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**A Randomised Controlled Trial of ‘Brief’ Smoking
Cessation Advice and NRT, delivered by Dental
Hygienists, to Patients in a Dental Setting**

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Thesis submitted for the degree of PhD to the Faculty of Medicine,
University of Glasgow.

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List of Abbreviations

AHCPR	Agency for Health Care Policy and Research
C	Control
CI	Confidence interval
CO	Carbon monoxide
COMMIT	Community Intervention Trial for Smoking Cessation
COPD	Chronic obstructive pulmonary disease
COT	Cotinine
CPD	Continuing Professional Development
CPITN	Community Periodontal Index of Treatment Need
DEPCAT	Carstairs Deprivation Categories
EIA	Enzyme immunoassay
ELISA	Enzyme-linked immunoabsorbent assay
ETS	Environmental tobacco smoke
EU	European Union
FTND	Fagerstrom Test for Nicotine Dependence
GC	Gas chromatography
GCF	Gingival crevicular fluid
GCMS	Gas chromatography-mass spectroscopy
GHS	General Household Survey
HSI	Heaviness of Smoking Index
I	Intervention
N/ELLE	Nicotelle
NHS	National Health Service
NIC	Nicorette
NICE	National Institute for Clinical Excellence
NOCS	Number of cigarettes smoked per day
NQ	Niquitin
NRT	Nicotine Replacement Therapy
OR	Odds Ratio
PATH	Partnership in Action on Tobacco and Health
PCD	Professionals Complementary to Dentistry
RCT	Randomised controlled trial
SD	Standard Deviation
SEG	Socio Economic Group
SHS	Scottish Health Survey
SRNT	Society for Research on Nicotine and Tobacco
ST	Smokeless tobacco
UK	United Kingdom
US	United States
USDHHS	United States Department of Health and Human Services
WHO	World Health Organisation

Declaration

This thesis is the original work of the author.

Vivian I Binnie BDS, MPH.

Summary

Tobacco use continues to be one of the UK's biggest health problems and smoking cessation is one area where health professionals can contribute towards the tobacco control agenda. The role that dental team members can play in the smoking cessation field is largely unevaluated. The work of this PhD thesis encompasses two phases, the first was to develop a means of determining smoking status, using analysis of cotinine, a nicotine metabolite. The second phase looked at the efficacy of dental hygienist-delivered smoking cessation advice in a dental setting.

The aim of the first study was to compare cotinine levels in different biological fluids collected from both smokers and non-smokers, and to relate the findings to self-reported smoking status. Patients recruited to the study were asked to provide samples of urine, blood and saliva (both stimulated and unstimulated). Data collected from patients by questionnaire included information on smoking behaviour, such as daily number of cigarettes smoked, and environmental exposure to smoke. Following sample collection, patients were asked to rate the acceptability of each sampling method. Samples were analysed using enzyme immunoassay (EIA) kits. In total, 80 patients participated, with 49 smokers and 31 non-smokers. There was clear differentiation between smokers and non-smokers ($p < 0.001$) for all the different samples in terms of cotinine concentration. A significant relationship was seen between cotinine levels and daily number of cigarettes for both salivas and urine (all $p < 0.001$) but not for serum. Participants found serum and urine collection methodologies 'very acceptable' (67% and 66%, respectively) whereas 9% found collection of stimulated saliva 'not at all acceptable'. Thus, cotinine, as analysed by EIA kits, whatever the collection method, shows good differentiation between smokers and non-smokers. Salivary samples have the advantage

of being non-invasive. However, collection methodology is important, as cotinine levels may vary.

The second and main phase of this PhD study aimed to examine the feasibility and efficacy of a smoking cessation randomised controlled trial, delivered by dental hygienists, in a cohort of periodontal patients attending an outpatient dental hospital department. Patients were randomised to receiving either smoking cessation advice based on the 5As and nicotine replacement therapy (NRT), or 'usual' care, where the patients allocated to the control group received 'very brief' advice from the recruiting consultant. At baseline, information was collected from 116 participants (59 intervention and 57 controls), on smoking history, level of nicotine dependence and motivation to quit. Patients also provided salivary samples for cotinine analysis, and exhaled air samples for carbon monoxide monitoring. At baseline, the mean age of trial participants was 41.2 years, 71% were female and half of the recruits (50%) were from the more deprived areas (DEPCATS 5-7). The median nicotine dependence score for trial participants (as measured by Fagerstrom Test for Nicotine Dependence) was 5, with a mean pack-years exposure of 21.5 and 24.8 years for the intervention and control groups respectively.

Point-prevalence quit rates are reported, verified by carbon monoxide and cotinine at 3 and 6 months, with cotinine verification at one year.

At 3 months, of the patients followed-up (102; 88%), 17.3% of the intervention group had quit, compared to 10.0% of the controls. Of patients recruited at baseline, 15.3% of the intervention group quit compared to 8.8% of controls.

At the 6-month time point, of the patients followed-up (71; 61%), 16.7% of the intervention group had quit, compared to 8.6% of the controls. Of the patients recruited at baseline, 10.2% of the intervention group had quit, compared to 5.3% of the controls. Prolonged abstinence figures would indicate that of the patients followed-up at 6 months, 11.1% of the intervention group had quit, compared to 8.6% of the controls. When prolonged abstinence is considered in terms of all recruited patients, the corresponding figures were 6.8% of the intervention group and 5.3% of the controls.

At 12 months, of the patients followed-up (56; 48%), 12.1% of the intervention group had quit, compared to 8.7% of the controls. Of the patients recruited at baseline, 6.8% of the intervention group had quit, compared to 3.5% of the controls.

With regards to secondary outcomes, those patients who were not successful in quitting were asked about changes in smoking behaviours. At 3 and 6 months, there was a statistically significant higher percentage of intervention participants who reported that they had made a quit attempt of one week or more in the preceding 3 months: 37% and 47% respectively for the intervention group, compared to 18% and 16% respectively for the control group. At 3 months, with regards to self-reported median reduction in number of cigarettes smoked daily, there was a statistically significant difference between intervention and control groups (33% v 0%). When self-reported reduction in smoking was associated with reduction in cotinine levels (reduction of smoking between baseline and 6 months), a statistically significant higher mean reduction was seen in the group who reported reducing smoking, compared to the group who reported that they had not reduced.

Using patients' self-reported 'Stage of Change' at baseline as a predictor of likelihood of quitting at 3 months, of the 14 biochemically validated quitters at this point, nine had classified themselves as being in the most ready state i.e. 'preparation stage' at baseline. With regards to using 'Stage of Change' as an outcome measure, where 'success' is considered to be positive movement through the model itself, at 3 months, there was no difference between intervention and control groups regarding numbers moving forward. At 6 months, there were slightly more individuals in the intervention group who moved forward compared to the controls.

With respect to efficacy, this thesis has shown that, given training in smoking cessation and access to NRT for their patients, dental hygienists in this secondary care setting can have a modest effect, with regards to the delivery of smoking cessation, at least in line with success rates reported by other health professionals. Further work needs to be carried out to determine the most appropriate model for future delivery of smoking cessation by dental team members.

Chapter 1 Introduction

1.1 General Introduction

Smoking has long been recognised as one of the most important preventable causes of ill-health and premature death, accounting for 13,000 smoking-related deaths per year in Scotland alone (Scottish Executive, 2004a). There are currently around 1.4 million smokers in Scotland, approximately 30% of the population. Comparable UK figures for tobacco-related disease are 120,000 deaths per year, with more than half dying from respiratory disease (Britton, 2004). The burden of disease caused by tobacco also has considerable financial implications. It is estimated that the NHS in Scotland spends up to £140 million every year on treating smoking-related disease (Scottish Executive, 2003a). However, tobacco is not only a UK but global problem, with tobacco use on the increase, especially in the developing countries (Abdullah and Husten, 2004).

The detrimental general health effects of smoking, such as lung cancer and heart disease are well known. Scotland unenviably has the highest lung cancer rate in Europe for both men and women (NHS Health Scotland and ASH Scotland, 2004). Tobacco use has strong links with deprivation, and is one of the main reasons why disadvantaged people are more likely to have poorer health and die younger (NHS Health Scotland and ASH Scotland, 2004). Around two-thirds of the social class differences in death rates in middle age are due to smoking. Smokers die, on average, 10 years earlier than non-smokers (Doll *et al.*, 2004).

While there is high public awareness of the general health risks of tobacco, there is much less public awareness of the association between smoking and oral problems such as oral cancer, or the links with periodontal disease. Scotland also has high rates of oral cancer, higher than in England, and this is largely due to the risk factor of smoking (Macpherson *et al.*, 2003).

The white paper, '*Smoking Kills*', released in 1998 (Department of Health, 1998), set out the UK agenda with regards to tobacco control. Following devolution, Scotland gained responsibility for her own health agenda, and since then, has followed her own (though often parallel with England) path with regards to tobacco control policy. The Tobacco Action Plan, released in 2004, aimed to move forward this agenda (Scottish Executive, 2004a). Key areas were identified, such as preventing young people from starting smoking, expanding smoking cessation services to help more smokers quit, and taking action around environmental tobacco smoke.

Smoking cessation is thus only one of the important strands in tobacco control. There is strong commitment to try to reduce the number of smokers and in particular to develop services to help them quit. It is known that 70% of smokers want to quit, though around 2% succeed in the long-term each year (NHS Health Scotland and ASH Scotland, 2004).

In the field of tobacco control, the volume of literature is vast. This review attempts to focus on the topics of most relevance to the study area described in this thesis, i.e. the development and planning of a smoking cessation intervention, as delivered by dental team members.

Information was retrieved from a variety of sources including librarian-delivered searches of Medline, self-delivered searches using PubMed, hand searches of relevant tobacco research journals and use of electronic sources such as Globalink.

1.2 Cigarette Smoking: an epidemiological overview

1.2.1 History of Tobacco Use

Tobacco (*Nicotiniana tabacum L.*), a native plant of the American continent, is believed to have been growing there since around 6000 BC (Tobacco Advisory Group of the Royal College of Physicians, 2000). Historians hold the view that American Indians started to use tobacco as early as the 1st century BC for medicinal and ceremonial purposes. By the 15th century, tobacco smoking was widespread among indigenous American people. By the end of that century, tobacco was introduced to Europe, with Christopher Columbus returning to the continent with it, received as a gift from American Indians (Borio, 2004).

Contrary to the popular myth that Sir Walter Raleigh was responsible for making smoking fashionable in Britain in the late 1500's, it was actually Captain Sir John Hawkins who first introduced tobacco into English society in 1565 (Borio, 2004).

During the 16th and 17th centuries, tobacco was commonly smoked in pipes and the habit was confined mainly to males in the upper echelons of society (Borio, 2004). One of the main reasons for the early growth in popularity of smoking tobacco was that it was thought to have healing properties. However, as early as 1604, King James VI of Scotland (I England) produced a damning report entitled '*Counterblaste to Tobacco*' in which he said that smoking was:

‘custome loathsome to the eye, hateful to the nose, harmful to the brain [and] dangerous to the lungs’ (James VI, 1604).

In an effort to discourage the habit, he increased the import tax on tobacco by 4000%, resulting in a dramatic decline in tobacco consumption (Borio, 2004). For economic reasons, however, this punitive tax was not maintained, thus leading to a rise in tobacco use again.

The first reference to the addictive nature of smoking was reported in 1610, when Sir Francis Bacon found it difficult to quit smoking.

‘the use of tobacco...conquers men with a certain secret pleasure, so that those who have once become accustomed thereto can hardly be restrained therefrom...’ (Bacon, 1622).

By the mid 1660’s tobacco use was common among all sectors of society and trade in tobacco between America and Europe had become a major business. The popularity of tobacco smoking continued to increase during the 18th and 19th centuries, particularly in the form of cigars rather than pipes. It was the invention of the manufactured cigarette, however, that transformed tobacco smoking into a mass habit. Cigarettes originated with British soldiers in the Crimean War (1853-1856) copying the habit of hand-rolling tobacco from their Turkish allies. The first cigarette factory opened in England in 1856, followed by the Wills factory in Bristol in 1871 and the Players factory in Nottingham in 1888 (Borio, 2004). These companies are still key suppliers in the tobacco industry today.

The scale of cigarette production was revolutionised in the 20th century by James Duke, a tobacco entrepreneur who introduced the use of cigarette-making machines (Hurt and Ebbert, 2002). Sales of manufactured cigarettes began to increase between 1895 and 1919 and continued to rise during World War I, when cigarettes were included in soldiers' rations. As a result, many soldiers returning home from the war were established regular smokers.

Until the advent of the Suffragette movement in the 1920's, it was socially unacceptable for women to smoke, but following this, substantial numbers of women started smoking and the tobacco industry responded by developing marketing strategies aimed at increasing the appeal of cigarettes to women. This resulted in a rapid escalation in cigarette smoking among both sexes during the 1930s and 1940s. By this time, the British tobacco epidemic was in full force.

1.2.2 UK Trends in Smoking Prevalence

1.2.2.1 Adult Trends in Smoking

Although no direct measures of smoking prevalence are available for the first half of the 20th century, it is thought that smoking rates in Great Britain changed dramatically over the last century. Using tobacco consumption as a proxy indicator, a peak consumption level of 8.8 g per head of population was seen in 1945/46 (Nicolaidis-Bouman *et al.*, 1993). At that time, an estimated 65% of men and 40% of women were regular smokers of manufactured cigarettes (Tobacco Advisory Group of the Royal College of Physicians, 2000).

In March 1962, when the Royal College of Physicians in England launched its landmark report into the tobacco epidemic entitled '*Smoking and Health*', it was estimated that 70% of men and 43% of women smoked (Royal College of Physicians, 1962).

Since 1972, smoking habits in Britain have been measured biennially, independently from the tobacco industry, as part of the *General Household Survey (GHS)*. This survey, at all time periods, includes a proportionally representative sample of the Scottish population.

In the first year of the GHS (1972), figures show that 52% of men and 41% of women were regular smokers in Great Britain (Office for National Statistics, 1998). The more recent trends from 1984 to 2002 have shown a fall in prevalence amongst men from 36% to 27% and a corresponding decreased rate amongst women from 32% to 25% (Office for National Statistics, 2004).

Over the same time period, similar trends were seen in Scotland, albeit rates were slightly higher. Prevalence amongst males fell from 43% in 1984 to 29% in 2002, with corresponding figures for women being 35% and 28% (Office for National Statistics, 2004).

Differences in smoking prevalence in Scotland are also apparent with regard to urban and rural areas. Adult smoking rates are higher in urban areas, with smoking being most common among adults living in Glasgow, Clackmannanshire, North Lanarkshire and West Lothian (each 35%) and least common in adults living in East Renfrewshire (17%) and East Dumbartonshire (19%) (Scottish Executive, 2003b).

Additional information concerning the smoking habits of the Scottish population is available from the results of the *Scottish Health Survey*, carried out in 1995 (Dong and Erens, 1997) and 1998 (Shaw *et al.*, 2000). This survey of the population of adults aged 16-74, living in private households in Scotland, aims to provide information about health and health-related behaviour, and is based on a larger sample size than the *General Household Survey*.

The 1995 *Scottish Health Survey* found that 35% of Scots (34% men and 36% women) smoked cigarettes (Dong and Erens, 1997). In this survey, self-reported smoking status was correlated with the participants' serum cotinine levels. Differences in the self-report and adjusted levels of smoking was most apparent in younger age groups, with 36% of males aged 16-24 years reporting that they smoked, compared with a biochemically validated figure of 45%. A similar but less marked relationship was found with the females, with a 33% self-reported smoking status being compared to a 36% level, as validated by serum cotinine measurements.

In the 1998 *Scottish Health Survey*, one third of adults (33%) aged 16-74 years self-reportedly smoked, with 34% of men and 32% of women saying that they used cigarettes (Shaw *et al.*, 2000). There was no change in prevalence for men between 1995 and 1998, though there was a reduction in smoking prevalence of 4% in women.

Self-reported smoking behaviour was highest for males aged 16-24 and 25-34 years, with a prevalence of 37% and 39% respectively. Prevalence gradually decreased with age, to 32% and 20% of men aged 55-64 and 65-74 years, respectively.

By contrast, there was no clear relationship between age and cigarette smoking rate for women aged between 16 and 64 years, with prevalence varying between 31% and 36%. However, a lower prevalence of 25% was seen in women aged 65-74 years.

In the 1998 survey, measures of self-reported smoking were verified by salivary rather than serum cotinine, in an attempt to increase the number of participants willing to provide biological samples for cotinine analysis. The findings were similar to those of the 1995 survey with regard to under-reporting, this again being most marked in the younger age-groups. Men aged 16-24 years under-reported smoking by 11%, as verified by cotinine. A similar trend was found in women in the 16-24 age group, with an under-reporting level of 7%.

Although the survey results found that smoking prevalence rates decreased with age, the prevalence of heavy smoking increased with age, with heavy smoking being defined as more than 20 cigarettes per day. Of those who smoked, only 35% of women were heavy smokers, compared to 42% of men. Additionally, more women (22%) were light smokers (<10 cigarettes per day) compared to men (18%).

A Scottish Office White Paper, '*Towards a Healthier Scotland*' (1999) set a target of a reduction to 33% (from 35%) of Scottish adults who smoke, by the year 2005. This was in fact achieved by 2001. A further target of reducing the percentage of the Scottish population still smoking to 29% by 2010 still stands (Scottish Executive, 2004a).

1.2.2.2 Trends in Smoking Rates in Children

Information on smoking rates in children in the UK is available via the survey '*Smoking, Drinking and Drug Misuse in Young People*' (The Scottish Office, 2000). The first survey was carried out in 1982 and has taken place biennially ever since. Results from the first Scottish study indicated that 29% of 15-year-old boys smoked, compared with 26% of girls. Prevalence for this age group peaked in 1996 with 30% of both boys and girls smoking.

In addition, further information on smoking amongst Scottish teenagers is available for children aged 11-15 years via the '*Health Behaviours of Scottish Schoolchildren*' (Todd *et al.*, 1999). In addition to smoking, these surveys looked at a variety of self-reported behaviours including, diet, exercise and toothbrushing.

These two surveys have been superseded by the '*Scottish Schools Adolescent Lifestyle and Substance Use Survey*' (SALSUS) which continues the biennial series of surveys used to monitor national trends in smoking, drinking and drug use in young people. The first survey using this format was carried out in 2002 (Currie *et al.*, 2003).

This study indicated that 8% of 13-year-olds and 20% of 15-year-olds reported regular smoking (>1 cigarette per week). In both age groups, girls were more likely to report being regular smokers than boys. Of the girls, 9% of 13-year-olds smoked, compared to 6% of 13-year-old boys. Prevalence rose with age, with 24% of 15-year-old girls smoking regularly, compared to 16% of 15-year-old boys.

When looking at patterns of smoking in 2002, 15-year-old boys reported smoking slightly more cigarettes per week than girls (38 v 34). With regard to dependency in this age group, the majority (71%) of regular smokers had been smoking for more than a year. Most pupils who smoked regularly reported that they would like to give up smoking (73% of those who had been smoking for > 1 year). Almost one third (32%) of regular smokers reported that it would be 'very difficult' to give up smoking altogether, with a further 36% indicating that it would be 'fairly difficult' to stop. Overall, of the regular smokers, 70% reported that they had tried to give up smoking.

National targets have been set for this group, with the aim being to reduce the proportion of 12-15 year olds who smoke from 14% (1995 level) to 12% by 2005 and to 11% by 2010 (The Scottish Office, 1999). Currently, around 12% of 12 to 15-year-olds smoke (Scottish Executive, 2004a).

1.2.2.3 Trends in Smoking amongst Pregnant Women

During the first antenatal hospital appointment, information is collected which allows measurement of the prevalence of women who smoke during pregnancy. Little change has been seen in the prevalence of women who smoke at the start of pregnancy over the 6-year period between 1995 and 2001, with prevalence dropping from 29% to 25% (Scottish Executive, 2001).

Pregnant women who smoke are seen to be a priority group and national targets have been set for a reduction from 29% (1995 level) to 23% and 20% by 2005 and 2010 respectively (The Scottish Office, 1998).

1.2.2.4 Risk Factors and Determinants of Cigarette Smoking

Gender, age and socioeconomic status all have a bearing on smoking prevalence.

a) Gender

The effect of gender on the likelihood of smoking is changing. As previously described, for most of the 20th century, smoking in Britain was more common in men. However, today, rates for adults are almost equivalent in males and females.

A trend towards increased female smoking rates has been evident for several years in schoolchildren, and the gap between the sexes has been increasing. Therefore, for some time, females have accounted for the majority of young smokers entering the smoking population. Future prevalence of smoking in young males and females will depend on uptake and cessation rates in both sexes during the later teenage years.

b) Age

Smoking is very uncommon in children up to and including the age of 11 years, but increases rapidly between the ages of 12 and 15. As previously described, among adults, smoking prevalence is greatest for men in the 25-34 age group and thereafter decreases progressively with age. For women, there is a lower prevalence in the older age group of 65-74 years.

c) Socioeconomic Status

Strong links are seen between smoking prevalence and socioeconomic status. Data extracted from the *General Household Survey* show trends in smoking by socioeconomic grouping (SEG) between 1976 and 1998 (Appendix 1).

There is a strong social gradient in prevalence of cigarette smoking, with those in manual social classes being much more likely to smoke than those in non-manual classes. In 1998, at the UK level, 15% of men and 14% of women in SEG 1 smoked compared to 45% of men and 33% of women in SEG 6.

For Scotland, data from the *Scottish Health Survey* also show a strong social class gradient in prevalence of cigarette smoking. In this study, The Registrar-General's classification of social grouping is used. In 1995, those from unskilled occupational groups were much more likely to smoke (58% men, 54% women) than those in professional occupations (17% men; 19% women). As shown in Appendix I, between 1995 and 1998, smoking prevalence among professional men reduced by 3%. A similar but more marked trend was exhibited by professional women, with a reduction of 10% between 1995 and 1998. Over the same time period, smoking prevalence in men from the unskilled occupations fell by 10% from 58% to 48%, whilst prevalence in women from the unskilled occupations actually increased, rising from 54% to 59%, i.e. 6 in 10 women in this social group used cigarettes.

When comparing figures from the Scottish Health Survey 1998 (Shaw *et al.*, 2000) with data from the General Household Survey 1998 (Office for National Statistics, 2000), with the exception of the professional occupations (SEG 1), smoking prevalence is higher in Scotland than the UK as a whole. This is most marked in women from the partly skilled /unskilled occupations.

While tobacco use has halved among the affluent, those living in the most deprived circumstances have continued to smoke at the same high rate as in the seventies.

Disadvantage, inequality and hardship experienced by low-income individuals causes them to be more likely to smoke than those from better-off families. Over 70% of two-parent households on Income Support buy cigarettes, spending about 15% of their disposable income on tobacco (Acheson, 1998).

1.3 Tobacco – Types of Product and Physiopharmacology

1.3.1 The Constituents of Cigarettes

Cigarettes are extremely well-designed and efficient delivery systems for enabling the speedy uptake of nicotine by the consumer.

Cigarettes consist of paper tubes containing chopped up tobacco leaf, usually with a filter at the mouth end. Cigarette tobacco is blended from two main leaf varieties; 'yellowish bright', also known as 'Virginia' which contains 2.5-3% nicotine and 'burley' tobacco which contains a higher nicotine level of 3-4% (British American Tobacco, 2004).

In addition to tobacco, cigarettes contain fillers made from the stem and other components of waste tobacco. These are mixed with water and flavourings such as vanilla to make the product more appealing to the consumer (British American Tobacco, 2004).

The nicotine and tar delivery can be modified by the type of paper used in the cigarette. The use of more porous paper allows more air to dilute the smoke, thus reducing the amount of tar and nicotine reaching the smoker's lungs. Filters are made of cellulose

and also trap some of the tar and smoke particles from the inhaled smoke. Filters also cool the smoke, making it easier to inhale.

1.3.2 The Constituents of Cigarette Smoke

Tobacco smoke consists of mainstream and sidestream smoke. Mainstream smoke is the smoke taken into the mouth by the smoker and sidestream smoke is the smoke which comes off the lit end of the cigarette. Many toxins are present in higher concentrations in sidestream smoke than in mainstream smoke, and nearly 85% of smoke in a room results from sidestream smoke (USDHHS, 1984).

Cigarette smoke is composed of volatile and particulate matter. Some 500 gases, including carbon monoxide, nitrogen, carbon dioxide, ammonia, hydrogen cyanide and benzene, have been identified in the volatile phase. This accounts for 95% of the weight of cigarette smoke, the other 5% being particulate (Tobacco Advisory Group of the Royal College of Physicians, 2000).

There are approximately 3,500 different compounds in the particulate phase, the major one being the alkaloid nicotine (Hoffman *et al.*, 1997). The particulate matter, without its alkaloid and water content, is called tar. Many carcinogens, including hydrocarbons and aromatic amines, have been identified in cigarette tar.

1.3.3 Nicotine Physiopharmacology

Nicotine is distilled from burning tobacco and small droplets of tar-containing nicotine are inhaled and deposited in the small airways and alveoli. Nicotine is a weak base and thus its absorption across cell membranes depends on the pH. When nicotine from

cigarette smoke reaches the small airways and alveoli, it is buffered to physiological pH and rapidly absorbed into the pulmonary alveolar and capillary circulation and then directly into the systemic arterial blood (Tobacco Advisory Group of the Royal College of Physicians, 2000).

From the time of smoking, it takes about 10-19 seconds for nicotine to reach the brain. Levels of nicotine in the plasma, as well as the brain, decline rapidly as a result of distribution to peripheral tissues. When smokers smoke throughout the day, there are oscillations between peak and trough plasma nicotine levels. However, because of its half-life of two hours, nicotine accumulates over 6-8 hours reaching levels in the plasma ranging from 20-40ng/ml which then fall progressively through the night (Benowitz *et al.*, 1982). There is considerable variation between people, both in their plasma nicotine levels and their intake of nicotine from a cigarette (Benowitz *et al.*, 1997). This can be manipulated by smokers who change their puff volume, the intensity of puffing and the depth of their inhalation.

Nicotine in mammals binds to the acetylcholine receptors in, amongst other regions of the central nervous system, the *ventral tegmental area* (Health Scotland and ASH Scotland, 2004). This leads to a burst of firing by cells in the *mesolimbic dopamine pathway* and release of a neurotransmitter called dopamine in the *nucleus accumbens*. This represents a basic '*teaching signal*' which in effect tells the animal to repeat the action that immediately precedes it. Thus nicotine is tapping into the basic and ancient '*reward pathway*' which evolved to enable animals to learn to adapt to a complex environment. Nicotine acts as a '*primary positive enforcer*'. Nicotine ingestion also leads to neuroadaptation so that when the body becomes depleted of nicotine, a range of

unpleasant physical and psychological withdrawal symptoms emerge. Nicotine withdrawal is discussed in Section 1.8.1.

1.3.4 Smokeless Tobacco

Smokeless tobacco (ST), which refers to both moist ground tobacco and chewing tobacco, is an important public health issue worldwide. This topic is currently at the protocol stage, awaiting a full Cochrane Review (Ebbert *et al.*, 2003).

Smokeless tobacco is especially important in the Indian sub-continent and in some areas of the UK with a high indigenous ethnic population. However, for the purposes of this literature review, a brief summary only will be presented, as it does not relate directly to the topic under study.

Smokeless tobacco can be defined as tobacco that is taken orally and so is not smoked. There is a huge variety of different types of tobacco being used globally, and it is not a homogenous product. Care, therefore, must be taken in comparing different types of tobacco and in interpreting different studies from various regions.

A national survey in the US reported that, among individuals aged 18 and over, 6.6% of males and 0.4% of females reportedly used ST 'in the last month' (USDHHS, 2001a). In India, an estimated 22% of males use ST solely and 8% use ST and smoked tobacco together (WHO, 1997). In the Sudan, about 40% of males and 10% of females use a type of ST known as Toombak (Idris *et al.*, 1994).

The main forms of smokeless tobacco include chewing tobacco of which there are many types in the US and Asia, particularly India. In this latter location, tobacco is often locally produced and can have other compounds added to improve flavour such as spices and sugars. Other added ingredients such as lime, betel and areca nut, have been shown to have potentially carcinogenic properties of their own (Merchant *et al.*, 2000; Phukan *et al.*, 2001). There is also a commercially produced form of tobacco known as paan masala.

With respect to the UK, the main users are predominantly members of the Indian, Pakistani and especially Bangladeshi communities. Recently, guidelines for health professionals including dentists were released in England, regarding delivery of smokeless tobacco cessation advice to those individuals who use this form of tobacco (West *et al.*, 2004).

In Europe, there is an oral type of snuff available in Sweden, known as snus. It is a moist, ground oral tobacco product that is typically placed behind the upper lip, either as loose ground tobacco or contained in sachets appearing like small tea bags. The snus is typically held in the mouth (without chewing) for approximately 30 min before being discarded. Approximately 30% of Swedish males are reported to use snus (Rodu *et al.*, 2002). The habit is particularly prevalent among young males and is rare in young women (Wickholm *et al.*, 2003).

Currently, within the EU, snus can only be legally sold in Sweden, though there is increasing interest in the role that it could play in harm reduction. At present, Sweden has the lowest rates of smoking amongst all European countries (around 17%) and is the

only country to have reached the World Health Organisation's goal of less than 20% daily smoking prevalence by the year 2000 (Fagerstrom and Schildt, 2003). There is some debate as to whether the existence and use of snus in this country has contributed to this low prevalence of cigarette use, and whether snus could be used as an aid to reduce or quit smoking (Gilljam and Galanti, 2003).

1.4 Tobacco Induced Conditions

The health concerns associated with tobacco use are widely known. A recent expansive and detailed 900-page report from the US Surgeon-General, entitled the 'The Health Consequences of Smoking' (USDHHS, 2004) aims to set out the current evidence-base with respect to tobacco use and its adverse health outcomes. The report particularly focuses on the concept of 'causality of association', and looks to standardise the approach to evidence in the form of (1) sufficient to infer a causal relationship, (2) suggestive but not sufficient to infer a causal relationship, (3) inadequate to infer the presence or absence of a relationship, or (4) suggestive of no causal relationship (USDHHS, 2004).

Amongst other conditions, the US report links smoking with cancer, cardiovascular disease and respiratory disease, and the body of evidence pertaining to these chapters is large and detailed. In this brief review, there is focus on the diseases and conditions which fall within category (1).

The US Surgeon General report specifies that smoking is causal in the following cancers: bladder, cervical, oesophageal, renal, laryngeal, lung, oral, pancreatic, stomach, and acute myeloid leukaemia.

With respect to cardiovascular disease, smoking is causal in abdominal aortic aneurism, atherosclerosis, coronary heart disease and stroke.

With regards to respiratory disease, tobacco use is causal in chronic obstructive pulmonary disease, pneumonia in adults and accelerated age-related decline in lung function. Smoking during childhood and adolescence produces significant respiratory health problems among young people including early onset symptoms including coughing and wheezing. With respect to respiratory disease in neonates, maternal smoking during pregnancy is associated with reduced lung function in infants.

In addition to the above serious health consequences, there are reproductive effects of smoking (British Medical Association, 2004). There are causal effects of sudden infant death syndrome and maternal smoking during pregnancy. Low birthweight, and premature rupture of the membranes leading to preterm delivery are also causal. Cleft lip and palate has also been linked with maternal smoking in the first trimester of pregnancy (Little *et al.*, 2004).

Smoking also leads to infertility in women (USDHHS, 2001b). The report lists other causal health outcomes: cataract, hip fracture, low bone density and peptic ulcer disease. The report also includes a section on the dental effects of smoking, including periodontal disease. These did not feature in the last report published in 1964.

1.5 Tobacco Induced Oral Conditions

Whilst many of the general health concerns associated with tobacco are well known, the detrimental effect of tobacco use on the mouth is less often acknowledged. Oral problems associated with smoking can range from cosmetic concerns such as staining and halitosis, through to conditions with significant morbidity and mortality.

Non-malignant smoking-related oral conditions are common in smokers and are discussed in Section 1.5.1.

Potentially malignant conditions are dealt with in Section 1.5.2, with oral cancer, possibly the most important disease to affect the oral cavity, being discussed in Section 1.5.3.

There is increasing interest being shown in tobacco use as a risk factor for periodontal disease, and this is covered in Section 1.5.4.

Smoking delays wound healing and one of the outcomes of this is increased rejection of dental implants. This is reviewed in Section 1.5.5.

1.5.1 Non-Malignant Smoking-Related Conditions

Aesthetic considerations include staining of the teeth, dental restorations and dentures, while side-effects of smoking include impairment of smell and taste, as well as halitosis (Johnson and Bain, 2000). With regard to oral mucosal conditions, nicotinic stomatitis, or smokers' palate, occurs in heavy smokers, especially those who smoke a pipe (Sham *et al.*, 2003). Melanic pigmentation (or smokers' melanosis) of the oral mucous membrane, especially on the attached gingivae, can be seen in 30% of heavy smokers

(Winn, 2001). There can also be overgrowth of the papillae on the dorsum of the tongue which can become stained with nicotine (black hairy tongue). All these conditions are not considered to be premalignant, and are reversible on smoking cessation (Reibel, 2003a).

In contrast to the conditions described above which are more prevalent in smokers, aphthae tend to occur less frequently in those who use tobacco (Tuzun *et al.*, 2000). Smoking cessation may result in an increase in the prevalence of aphthous ulcers and this can be a temporary, if unpleasant, side effect of quitting (Ussher *et al.*, 2003).

1.5.2 Potentially Malignant lesions

1.5.2.1 Leukoplakia

Of the potentially malignant lesions of the mucous membrane, leukoplakia or white patches are the most common type. Leukoplakia can be defined as a 'white patch that cannot be characterised clinically or pathologically as any other disease' (Kramer *et al.*, 1978). It is a clinical term and has no histological connotations (Lamey and Lewis, 1997). The clinical presentation of leukoplakia can vary from minimal localised lesions to extensive involvement of the mucosa.

The prevalence of leukoplakia can vary among populations, often being between 1 and 6% (Lim *et al.*, 2003). Leukoplakia is associated with the risk factors of tobacco and alcohol (Van der Waal *et al.*, 1997), and can occur six times more frequently in smokers than non-smokers (Baric *et al.*, 1982). There seems to be a strong relationship between smoking and the development of leukoplakias in the floor of the mouth (Schepman *et al.*, 2001).

There is debate around the malignant transformation rate of leukoplakia to oral cancer, with some researchers stating a rate of around 0.6% to 5% annually (Silvermann *et al.*, 1984; Lee *et al.*, 2000, Greenspan and Jordan, 2004), and others reporting a higher rate of 15% (Tradati *et al.*, 1997).

Reducing or cessation of tobacco use may result in the disappearance of leukoplakia (Gupta *et al.*, 1986; Chad-Martin *et al.*, 1999).

1.5.2.2 Erythroplakia and Speckled Leukoplakia

Erythroplakia (red patches) and speckled leukoplakia (white patches with a red component) are much less common in the population than leukoplakia. Studies quote a prevalence of 0.09% to 0.83% (Hashibe *et al.*, 2000). Erythroplakia are red lesions, velvety in texture and the margins may be sharply defined (Cawson and Odell, 2002). Speckled leukoplakia consist of white flecks or fine nodules on an atrophic erythematous base. They can be considered to be a transition between leukoplakia and erythroplakia (Cawson and Odell, 2002).

Both erythroplakia and speckled leukoplakia should be viewed with greater suspicion than leukoplakia, having a much higher potential for development of cancer. Estimates of malignant transformation rates vary, with one study finding 91% of lesions to be either dysplasia, carcinoma *in situ* or cancer (Shafer and Waldron, 1975), while another found that 20% of cases progressed to cancer within 10 years, despite treatment (Trock, 2000).

1.5.2.3 Oral Candidosis

It is now thought that smoking, either alone or in combination with other factors, appears to be a predisposing factor for oral candidosis. After antimycotic therapy, the condition may relapse if the patient continues to smoke, though there may be instances where the condition disappears with no drug treatment following smoking cessation (Johnson and Bain, 2000). It is thought that candidal infection not only causes epithelial hyperplasia, but may also induce epithelial atypia, leading to malignant change (Sitheeque and Samaranayake, 2003). It is not clear whether candidal infections are a cause of leukoplakia or whether there is a superimposed infection in a pre-existing lesion (Cawson and Binnie, 1980; Reibel, 2003b).

1.5.3 Oral Cancer

Approximately 90% of oral cancers are squamous cell carcinomas (Neville and Day, 2002). The most common oral cancer sites are the tongue and floor of mouth (Johnson *et al.*, 1993). In addition, oral cancer patients have an increased likelihood of developing a second primary tumour elsewhere in the aerodigestive tract (Crosher and McIlroy, 1998).

1.5.3.1 Tobacco as a Risk Factor for Oral Cancer

Smoking is a key risk factor for the development of oral cancer. Tobacco smoke has a direct carcinogenic effect on the epithelial cells of the oral mucous membranes (EU Working Group on Tobacco and Oral Health, 2000). In recent years, much attention has been given to smoking-related mutations in a tumour suppressor gene coding for the protein p53. This protein is important in regulating cell proliferation and has a role in the repair of DNA damage (Nylander *et al.*, 2000).

There has been a well-demonstrated dose-response relationship for tobacco use and risk of development of oral cancer, with the risk significantly increasing with the number of cigarettes smoked and the duration of smoking (La Vecchia *et al.*, 1997). Individuals who smoke and do not drink alcohol, have a two to four-fold increased risk of developing oral cancer (Johnson and Bain, 2000; Winn, 2001). When the risk factor of alcohol is added into the equation, the relationship becomes synergistic, with a smoker who consumes two packs of cigarettes and take more than four alcoholic drinks per day, having a 35-fold increased risk of oral cancer development (Blot *et al.*, 1988).

However, increasing interest is being shown in the higher reported number of cases presenting at an earlier age and their likely aetiological factors (Rodriguez *et al.*, 2004). A study in the south east of England, looking at survivors of oral cancer (aged under 45 years), found that a quarter of the cases had no links to the traditional risk factors of tobacco and alcohol (Llewellyn *et al.*, 2003). Likewise, in a survey of 38 oral and pharyngeal cancers in Scotland, 32% of cases described themselves as never-smokers and 13% as never-drinkers (Mackenzie *et al.*, 2000). Thus, whilst tobacco use remains the major risk factor for oral cancer generally, further studies are required to look more closely at other possible aetiological factors and mechanisms of development including genetic susceptibility, viral, psychological and occupational variables.

With respect to smokeless tobacco, the product, as used by the Pakistani and especially Bangladeshi communities, carries with it an increased risk of oral cancer (West *et al.*, 2004). The most commonly used form is tobacco mixed with lime, with additional psychoactive compounds such as areca nut. The resulting quid is chewed or held in the mouth. In the US and Sweden, smokeless tobacco in the form of snuff is used. Snuff

habits as used in these countries carry lowered but still important risk of serious health hazards, including oral cancer (Johnson, 2001). Further information on all types of smokeless tobacco is to be found in Section 1.3.4.

1.5.3.2 Incidence of Oral Cancer

With regards to the epidemiology of oral cancer, its incidence varies markedly worldwide. Globally, it is the sixth most common malignant tumour for both genders (Johnson, 2001). There are high rates in the Indian subcontinent, where it accounts for up to 40% of all malignancies (Johnson, 2001). This figure is related to ethnic and religious practices regarding the use of smokeless tobacco. In Scotland and the UK, such products are limited to the relevant ethnic groups (Khan *et al.*, 2000).

When looking at European incidence rates, France has the highest level of oral cancer, and this is related to high smoking and alcohol intake levels (Andre *et al.*, 1995). With regards to incidence in Scotland, currently, around 500 new cases of oral cancer are diagnosed each year (Macpherson *et al.*, 2003).

In Scotland, oral cancer is twice as common amongst males as females, and the incidence rate of approximately 12 per 100,000 in males and 5 per 100,000 in females is almost double the rates in England (Quinn *et al.*, 2001). Approximately 85% of new cases occur in people aged 50 and over. There is a clear association between social deprivation and incidence rates of oral cancer (Macpherson *et al.*, 2003). This relationship is stronger in males. There has also been an increase in the number of cases over the last 30 years, and this may be linked to patterns of smoking and alcohol consumption.

1.5.3.3 Tobacco-Related Advice Concerning the Prevention of Oral Cancer

Information to the general public concerning the prevention of oral cancer includes advice not to smoke, or if a current tobacco user, to give up smoking, and to drink within accepted limits (Macpherson *et al.*, 2000). It has been reported that cessation of smoking eliminates the increased risk of development of oral cancer within 5-10 years (Blot *et al.*, 1988).

1.5.4 Periodontal Disease

1.5.4.1 Relationship Between Smoking and Periodontal Disease

In recent years, the relationship between smoking and periodontal disease has been investigated extensively, with over 200 papers appearing in the literature during the past few years (Rivera-Hidalgo, 2003). Reviews of this body of work indicate that there is strong evidence from cross-sectional, case-control and other longitudinal studies that smokers are more likely to be affected by periodontitis than non-smokers and that response to periodontal therapy is compromised in the former group (Kinane and Chestnutt, 2000; Johnson and Slach, 2001; Rivera-Hidalgo, 2003; Johnson and Hill, 2004).

The evidence shows that, in general, smokers are approximately three times more likely than non-smokers to have periodontitis and that the relationship between smoking and periodontitis is even stronger among those more severely affected by the disease (Johnson and Hill, 2004). For example, a large US-based epidemiological study reported recently that for adults aged 20-49 years, the odds ratio of attachment loss associated with current smoking was 2.29 for loss of up to 2mm, but for attachment loss of at least 3mm, the odds ratio was over 18 (Hyman and Reid, 2003).

Recent reviews of the smoking-related periodontal literature indicate that numerous studies show that, after adjusting for plaque levels, smokers have more severe bone loss, more attachment loss, deeper probing depths and fewer teeth than non-smokers (Rivera-Hidalgo, 2003; Hilgers and Kinane, 2004; Johnson and Hill, 2004).

The case for smoking being an important risk factor for periodontal disease is further strengthened by the fact that a dose-response relationship is seen between the number of cigarettes smoked and the severity of periodontal disease. Grossi et al. (1995), in a study involving 1361 adults, found that in relation to the risk of experiencing severe bone loss, the odds ratio ranged from 3.25 to 7.28 for light and heavy smokers respectively. A similar dose-response relationship has been seen in other studies (Norderyd and Hugoson, 1998; Bergstrom, 2003).

1.5.4.2 Sociological factors and Periodontal Disease

A case-control study of the relationship between life events and periodontitis has shown smoking to be statistically associated with periodontal disease, after controlling for oral health behaviours and sociodemographic variables (Croucher *et al.*, 1997). This work confirmed earlier findings that periodontal disease experience is influenced by social and behavioural factors, and that smoking is independent of other factors (Locker and Leake, 1993).

1.5.4.3 Pathogenic Effects of Smoking

With regard to the pathogenic effects of smoking on the periodontal tissues, a number of mechanisms are thought to be involved. These include direct damage to the tissues from smoking-related toxins, changes to the microbial composition of subgingival

plaque, alterations to the host innate and immune responses to plaque and changes to tissue vasculature influencing blood flow (Kinane and Chestnutt, 2000; Johnson and Slach, 2001; Rivera-Hidalgo, 2003; Johnson and Hill, 2004; Hilgers and Kinane, 2004). These theories and proposed mechanisms result from a vast amount of work in this area in recent years. There is still ongoing debate and controversy in relation to some of these areas, e.g. the effect on the plaque microflora, and studies into the specific effects of smoking on the host's inflammatory and immune responses continue to be very active areas of research. An in-depth review of this literature is outwith the scope of this thesis.

1.5.4.4 Effects of Smoking Cessation on Periodontal Status

Importantly, the literature provides evidence that stopping smoking can have a positive impact on periodontal status (Hilgers and Kinane, 2004), with the progression of the rate of periodontal destruction decreasing following smoking cessation and recent non-smokers responding to periodontal treatment in a manner similar to that of non-smokers (Johnson and Hill, 2004).

1.5.4.5 Effects of Smoking on Periodontal Treatment Outcome

It has been reported that poorer outcome to periodontal treatment, both mechanical and surgical, occur in smokers compared to non-smokers (Grossi *et al.*, 1997; Kinane and Radvar, 1997; Scabbia *et al.*, 2001). These poorer outcomes extend also to oral surgery with Meechan and co-workers (1988) showing, in a large sample of extraction patients, significant reductions in post-extraction socket blood fill and more painful extraction sockets in tobacco users.

1.5.4.6 Cotinine and Periodontal Disease

Relatively few studies have looked at the relationship between cotinine and periodontal disease. Gonzalez and co-workers (1996) found that the severity of bone destruction in periodontal disease, as measured either as clinical attachment level or crestal bone height, was positively correlated with serum cotinine levels. Similarly, Machtei *et al.* (1997) found that the severity of periodontal attachment loss was positively correlated with serum cotinine levels.

Gunsoley and co-workers (1998) looked at patients who had minimal periodontal destruction and found that smoking patients, as verified by serum cotinine, showed greater levels of recession. However, by contrast, Chen *et al.* (2001) found neither salivary cotinine concentration, nor GCF cotinine levels to be significantly correlated with probing depth, attachment loss or tooth loss.

1.5.5 Effect of Tobacco Use on Dental Implants

Johnson and Hill (2004) report that the majority of studies show the failure rate of implants in smokers to be at least twice that in non-smokers. Wallace (2000) found a failure rate after four year of 16.6% in smokers, compared to 6.9% in non-smokers, with increased failure rates in smokers also having previously been reported by other researchers including Bain and Moy (1993) and De Bruyn and Collaert (1994).

The impact of smoking on implant failure rates is not equal for upper and lower jaws, with a much higher rate being associated with the maxilla. For the maxilla, Bain and Moy (1993) reported failure rates of 17.9% and 7.3% in smokers and non-smokers

respectively. There was less of a difference in the mandible, with a failure rate of 4.6% in smokers and 2.4% in non-smokers.

Bain (2001) emphasised the importance of quitting smoking in his analysis of 223 Branemark implants in 78 patients. In this prospective study, smokers were requested to quit smoking for 9 weeks; one week prior to surgery and for eight weeks thereafter. Of the 57 smokers who underwent surgery, 51 (89.5%) started on the cessation protocol and 48 (84.2%) completed the nine weeks without smoking. It was shown that there was a statistically significant higher failure rate in smokers compared to non-smoking controls and quitters. However, there was no statistically significant difference in failure rates between non-smokers and quitters. When looking at the longer-term smoking cessation outcomes at 3 months, 6 months and 1 year, the success rates were 70.2%, 43.9% and 40.4% respectively. However, these outcomes were not biochemically validated by cotinine.

1.6 Overview of Tobacco Control

Smoking cessation interventions targeting individual smokers (the research area of this thesis) are only part of a much broader spectrum of strategies which comprise the tobacco control agenda.

Recently, there have been some major developments in this area with the production of a treaty addressing tobacco as a global public health problem. In 2003, WHO developed the *First Framework Convention on Tobacco Control*, which has been adopted by a number of member countries (WHO, 2003). The framework covers a wide range of

issues including measures relating to the demand for and the supply of tobacco (Shibuya *et al.*, 2003).

The first series of recommendations within the framework look at reducing the demand for tobacco products. Another major area of importance addresses the issue of environmental tobacco smoke and looks at enabling the legislation and public health agenda in encouraging public places and workplaces to be smoke-free (Scottish Executive, 2004b). Restrictions of this kind are thought to increase the number of smokers who quit, as well as providing protection for others from passive smoking. Ireland recently banned smoking in public places (1 April 2004) and Scotland is currently looking at introducing this public health measure.

A further area addressed in the framework is the price of tobacco, as this is thought to be one of the strongest influences on tobacco consumption. In the UK, an increase in price of tobacco products of 10% has been found to cause a fall in smoking of 4% in adults and 6% in children, thus reducing prevalence while increasing revenue (Jamrozik, 2004).

Public education, including general and school education, as well as the use of mass media have a direct influence on prevalence of smoking and are most effective when delivered as part of a comprehensive tobacco control policy (NHS Health Scotland and ASH Scotland, 2004). The recent round of advertising by the British Heart Foundation, using a visual dripping cigarette, led to very high awareness of the message by the general public (British Heart Foundation, 2004).

Comprehensive bans and restrictions on tobacco advertising, promotion and sponsorship are important strands of a tobacco control policy (Saffer and Chaloupka, 2000). Norway was the first country to ban tobacco advertising (1970), whereas in the UK, tobacco advertising has only been banned from 14 February 2003 (Jamrozik, 2004). Indirect advertising, for example, sponsorship of sports such as motor racing is due to end in 2006 and is just as important as the direct form of advertising. Equally important, are promotion of tobacco products through product placement in film and other media (Sargent *et al.*, 2001). Point-of-sale advertising also needs to be closely monitored and banned, with preferably legislation adopted which requires tobacco products to be stored out-of-sight, underneath the counter (Scottish Executive, 2004a).

Regulation of tobacco products is a thorny area. Cigarettes are highly toxic, though in most countries, they have remained exempt from food, drug or consumer protection legislation. Smokeless tobacco, though safer, is banned on health grounds in all EU countries with the exception of Sweden, whereas medicinal nicotine, in the form of patches or other products, is subject to drug legislation and the accompanying restrictions.

Cigarette packaging and labelling is a further issue, with increasingly visible and visual warnings about the dangers of cigarettes being adopted as standard in many countries (Aftab *et al.*, 1999). Canada was the first to lead with visual warning including graphic pictures of oral cancer. Currently in the UK, text-only warnings are being used.

There are two measures which relate to reducing the supply of tobacco. The first is elimination of the illicit trade of tobacco products and the UK government is committed

to trying to reduce this (HM Customs and Excise, 2000). The second area for attention is the restriction of sales to and by minors (under 16s). In Scotland, test-marketing schemes have been set up to ensure shopkeepers are not disregarding the law (NHS Health Scotland and ASH Scotland, 2004).

One further strand of policy, emphasised by the WHO Framework, and of particular relevance to the developing world, is to address the problem of finding economically viable alternatives for the current tobacco growers to plant and harvest, to ensure their economic survival.

Tobacco cessation and dependence measures which help treat smokers are discussed elsewhere in this chapter (Sections 1.9 and 1.10).

1.7 Measurement of Smoking Status

There are two main methods of determining smoking status. The first method, known as self-report, involves asking the individual. The second method is to use some form of biomarker to validate the information given by the individual. It is now generally accepted that in smoking cessation trials, it is essential to use some form of biochemical validation (Gariti *et al.*, 2002).

1.7.1 Self-Report

When asking about an individual's recent exposure to tobacco, questionnaires are often used to determine cigarette intake and environmental exposure. The use of pack-years is discussed in Section 1.7.2 below.

In addition, self-report can be used to determine whether an individual has stopped smoking, or not. Once this information has been collected, there are a number of ways of using this information to determine abstinence, and these measures are discussed in Section 1.7.3 below.

1.7.2 Self-Reported Pack-Years

Another use of self-report is to measure a person's lifetime exposure to tobacco products over a number of years. One method of measuring this is the use of 'pack-years' (Alpagot *et al.*, 1996). Self-reported data obtained from the patient, assessing the number of cigarette packs (20 cigarettes per pack) smoked per day for a number of years can be used to categorise the risk into high, medium and low. Weighed pack-years can also be utilised in order to allow for hand rolled cigarette consumption (Schlecht *et al.*, 1999). There is use of this measure in the dental literature, particularly periodontally-related, and in coronary care and respiratory medicine (Chen *et al.*, 2001; Chambless *et al.*, 2003; Patel *et al.*, 2004).

1.7.3 Measures of Abstinence in Smoking Cessation Trials

Self-report can be used as a means of determining smoking status after a smoking cessation intervention (Velicer *et al.*, 1992; Velicer and Prochaska, 2004). There are three measures which can be used: point prevalence, prolonged abstinence and continued abstinence. These three measures are discussed below.

Point prevalence abstinence can be defined as the proportion of subjects not smoking at a point in time.

Prolonged abstinence is defined as the proportion of participants not smoking after an initial grace period where the smoker is allowed to lapse, usually one or two weeks just after the quit date.

Continuous abstinence is defined as the proportion of people not smoking at all since the occurrence of the intervention or critical event such as the quit date.

The arguments for using point prevalence include the fact that biochemical validation of this measure is possible, depending on the timeframe selected (Velicer and Prochaska, 2004). In addition, point prevalence measures are often collected, and can contribute to a meta-analysis. Point prevalence rates, if measured sometime after the event or intervention, such as 6 or 12 months, can include smokers who take delayed action and quit. Therefore, they also tend to be more accurate in that the immediacy of the measure does not rely on participants self-reported recall of smoking some time previously, as in prolonged abstinence (Velicer and Prochaska, 2004). The disadvantages of point prevalence include the fact that this measure is not as stable as continuous abstinence, and given the high rate of relapse during the first 3 months following quitting, it is predictable that individuals who are counted as former smokers at one point in time, will be current smokers at the next point in time.

Prolonged abstinence measures reflect a combination of continuous and point prevalence abstinence rates. Individuals are counted as former smokers if they have been continuously abstinent for a prolonged period of time, such as 3, 6 or 12 months. Prolonged abstinence rates are able to include people who make delayed or repeated quit attempts following an intervention. This measure also allows smokers a grace

period, and is thought to more accurately reflect what happens during smoking cessation. Research has shown that a number of trial participants who successfully quit, may have a lapse very early on in the quit attempt (Hughes *et al.*, 1992). By including a grace period, this allows for this smoking behaviour, without automatically counting this behaviour as a failure.

Continuous Abstinence is the strictest measure and allows no smoking from the quit date. The advantage of this measure is that it is more stable over time and across studies than point prevalence rates. The longer the period of continuous absence, the less the probability of relapse. This measure has a number of disadvantages which include a requirement that the point of intervention has to be clearly defined. This may be possible in a pharmacological study, but is much more difficult in a self-help study where the timing of a cessation attempt is under the control of the subject. Also few smokers make the transition to non-smokers without any lapses and relapses (Velicer and Prochaska, 2004).

Trials may vary in the measures they report. Hughes and co-workers (2003) recommend that trials report multiple measures of abstinence, and as a minimum, smoking cessation trials should report prolonged abstinence as the preferred measure, coupled with point prevalence as the secondary measure. Two trials reporting recently used continuous absence and point prevalence (Molyneux *et al.*, 2003; Tonneson *et al.*, 2003), whereas another used sustained absence and point prevalence (Borland *et al.*, 2003). Hughes *et al.*, (2003) do not recommend the use of the term sustained abstinence.

1.7.4 Use of Biomarkers in Measuring Tobacco Smoke and Environmental Tobacco Smoke

Assays can provide measurement of the concentration of substances in biological tissues and secretions. An example of this is the level of a tobacco constituent in exhaled air, saliva, blood, urine, hair or other body part (Shields, 2002). Such biomarkers can be used to determine internal exposure, estimate a biologically effective dose or used to determine the level of potential harm that a compound may have. They are of importance in many fields, but this review confines itself to those of relevance as validators of smoking status in cessation trials (Gariti *et al.*, 2002; Rebagliato, 2002). Examples of such biomarkers are cotinine and nicotine levels in a variety of tissues including blood and saliva, and carbon monoxide measurements in exhaled air.

Additionally, biomarkers such as cotinine can be used to determine an individual's exposure to passive or environmental tobacco smoke (ETS) (Benowitz, 1996; Philips *et al.*, 1999).

1.7.5 Cotinine

Some studies have used nicotine to measure tobacco exposure. However, as nicotine has a short half-life of around 2 hours, results are very dependent on time of sampling (Feyerabend and Russell, 1990; Benowitz, 1999). Thus, while nicotine levels may be measured, this is usually in conjunction with another means of testing exposure.

Cotinine, a metabolite of nicotine, is currently regarded as the best biomarker for exposure to tobacco smoke (Rebagliato, 2002). Since the early 1980's, it has been used to determine an individual's exposure to tobacco (Feyerabend and Russell, 1980). It is distributed throughout extracellular fluid and is excreted through the kidneys and

salivary glands (Benowitz, 1982). Cotinine has a half-life of approximately 20 hours and is gradually excreted from the body over 3-4 days (Jarvis *et al.*, 1988).

As a biomarker, cotinine has the advantage of being almost specific to tobacco smoke. There are, however, a number of exceptions, including occupational exposure to tobacco leaves, particularly during harvesting (Quandt *et al.*, 2001), the use of smokeless tobacco (Andersson *et al.*, 1994) and the use of nicotine replacement therapy, including gum, patches and other smoking cessation aids. Additionally, low levels of cotinine have been found in the diet, particularly in vegetables such as tomatoes, cauliflower and black tea. However, the dietary impact from such foodstuffs on cotinine levels can be regarded as insignificant (Benowitz, 1999).

1.7.5.1 Choice of Biological Sample for Cotinine Sampling

Cotinine can be measured in a variety of body constituents including blood, urine, saliva, amniotic fluid, cervical mucus and hair (Vine *et al.*, 1993; Poppe *et al.*, 1995). The choice of sample may depend on a number of factors including the setting in which the study or intervention takes place and the acceptability of the method of collection to both participants and the professionals undertaking the work.

Blood or serum is often the sample of choice, especially when a sample of blood is taken for routine purposes, such as in antenatal clinics (Tappin *et al.*, 2000). Urine collection is easier in some settings such as schools and worksites, though there may be some concerns about detecting illicit drug use (Leiria *et al.*, 1999). In such circumstances, salivary collection may be preferable (Etzet, 1990). A review of the types of biological samples used for measurement of cotinine is detailed in Chapter 2.

1.7.5.2 Methods of Analysis of Cotinine

Several chromatographic methods have been used for the analysis of cotinine: gas chromatography (GC) (McAdams and Cordeiro, 1993), gas chromatography-mass spectroscopy (GCMS) (Shin *et al.*, 2002; Torano and van Kan, 2003) and liquid chromatography-mass spectroscopy (LCMS) (Bernert *et al.*, 2000).

The advantages of GC-based methodologies include accuracy: with higher levels of sensitivity and specificity than other methods, especially when looking at levels of exposure associated with passive smoking. Such assays can also deal rapidly with large sample numbers. One disadvantage of chromatographic-based methods of analysis, however, is cost. This is due to the high capital costs of the equipment required and the time involved in preparation and extraction of the materials.

A number of immunoassays, including radioimmunoassay (RIA), have also been used for cotinine analysis. More recently, enzyme-linked immunoabsorbant assay (ELISA) kits have become available both in the US (OraSure) and UK (Cozart). The kits are largely unevaluated in the UK. The advantages of the kits include accessibility; they do not require costly equipment and are relatively easy to handle. A fuller discussion of the advantages and disadvantages of the kits is given in Chapter 2.

A number of studies have compared the different methods of analysing cotinine. A study, comparing ELISA screening kits with gas chromatography-mass spectrometry and using urine samples, found conflicting results depending on the laboratory used for analysis.

An initial study found poor agreement with the two methods of analysis (Gariti *et al.*, 2002). However, in a later study, samples from the same patients were analysed blind (Alterman *et al.*, 2002) and on this occasion the ELISA results showed almost total agreement with the GCMS findings.

1.7.5.3 Determining Cut-Offs for Smokers/Non-Smokers

Studies comparing non-smokers and smokers have consistently found that measurement of cotinine in urine, serum or saliva can distinguish active smokers from non-smokers. Active smokers almost always have serum or saliva levels higher than 15ng/ml and sometimes greater than 500ng/ml. Non-exposed, non-smokers have cotinine levels of < 1ng/ml with non-smokers exposed to ETS having levels of cotinine in the range of 1-15ng/ml (Rebagliato, 2002). Difficulty may arise in differentiating between a non-smoker, who is heavily exposed to ETS, and a light, occasional smoker.

Self-reported non-smokers, who seem to be smokers on the basis of biochemical measurements, are generally considered 'deceivers' of their true smoking status (Archbold *et al.*, 1995).

When making comparisons of levels of self-reported smoking misclassification across studies, it can be difficult to directly compare results because of differences in a) analytical techniques (gas chromatography compared with radioimmunoassay) and b) populations studied (Rebagliato, 2002).

A study investigating the effect of ethnicity, found that serum cotinine levels were higher amongst black smokers than white or Mexican American smokers (Caraballo *et al.*, 1998). This was thought to be due to slower clearance rates in black smokers and a higher nicotine intake per cigarette in this population (Perez-Stable *et al.*, 1998).

1.7.5.4 Near-Patient Testing of Cotinine

A disadvantage of the cotinine assay method outlined above is that instant feedback to the patient is not possible. One new technique, attempting to address this issue, is the development of a 10-minute disposable near-patient saliva test. This consists of a plastic device, containing dried reagents to measure nicotine and its cotinine metabolite, by a colorimetric assay (Cope *et al.*, 2000). This technique gives a semi-quantitative assessment of tobacco consumption by monitoring the colour change in the sample and by comparing it to a reference chart and the results can be fed back to the patient. Alternatively, the test can be quantified by measuring the light absorbency with a colorimeter and a concentration of nicotinic metabolites obtained with reference to a cotinine standard. With this latter technique, however, instant feedback to the patient is lost. A similar test exists for use with urine (Cope *et al.*, 1996). As they are relatively new to the market, their full potential has still to be determined.

1.7.6 Carbon Monoxide (CO)

The most widely used biomarker, both to determine tobacco exposure, and to biochemically validate quitting in smoking cessation interventions, is carbon monoxide (CO) (Middleton, 2000). Exhaled air samples are measured for CO using a hand-held monitor.

The advantages of using such a monitor include economic considerations, with such equipment being much cheaper per head to use than cotinine sampling (Jarvis *et al.*, 1986). Additionally, these monitors are not difficult to manipulate and staff can easily be trained to use them. The readings can also be taken quickly and the CO measurement fed back to the patient. This can be an important motivational tool to use during a patient's quit attempt (Hajek and Belcher, 1991). Other advantages include its use to verify smoking status when the individual is using some form of nicotine replacement therapy (Scott *et al.*, 2001).

Limitations of CO readings include the fact that they are not specific for tobacco, as there are a number of non-tobacco sources, such as vehicle exhaust fumes, which might affect levels, especially in urban areas. Carbon monoxide also has a short half-life of 4-5 hours, so cannot detect a patient's exposure over a longer time period.

There is also some debate as to the cut-off level to be used to differentiate smokers from occasional smokers and non-smokers. A cut-off of between 6 and 10ppm is often used (Gariti *et al.*, 2002; Tonnesen *et al.*, 2003).

A number of papers comparing the specificity and sensitivity of methods using carbon monoxide and cotinine assays are discussed in Section 1.7.7.

1.7.7 Comparison of Different Methods used to Determine Smoking Status

A key issue for smoking cessation researchers concerns the confirmation of self-reported abstinence. A relatively small inflation in abstinence rates, determined by self-report, that is not biochemically validated, can have significant implications for the evaluation of the efficacy of a given treatment (Gariti *et al.*, 2002).

A number of studies have compared the use of carbon monoxide, cotinine and self-report (Murray *et al.*, 2002). In one of the first (Murray *et al.*, 1993), at one-year follow-up, cotinine and carbon monoxide monitoring detected smoking in 17% and 10% respectively of self-reported non-smokers. This large, population-based study, the 'Lung Health Study', was a randomised trial in 10 centres, involving 3923 participants in a smoking cessation programme and 1964 usual-care participants. Smoking was assessed at the first annual check-up. Sensitivity (percentage of smokers detected) and specificity (percentage of non-smokers detected) were calculated by comparing each biochemical measure with the self-report. For cotinine compared with self-report, the sensitivity was 99.0% and the specificity was 91.5%. For carbon monoxide compared with self-report, the sensitivity was 93.7% and the specificity was 87.2%.

A smaller, though more recent study, examined smoking cessation outcomes in a group of 240 participants who had participated in a trial that compared the efficacy of different intensities of psychosocial treatments, coupled with 8 weeks of patch treatment (Gariti *et al.*, 2002). Treatment outcomes were assessed 9, 26 and 52 weeks from initial treatment, and data on self-report, carbon monoxide and urinary cotinine were collected. Carbon monoxide measurements taken at 9 weeks found two (1.9%) trial participants who reported being non-smokers, with readings at the level consistent with exposure to

tobacco smoke. Cotinine measurements detected a higher yield of 22 (23.2%) who could be classified as being ‘deceivers’. There were similar, if less marked, findings at 26 weeks (1.6% and 14.8%) and at the 1-year interval (1.7% and 6.8%). The authors concluded that cotinine analysis was by far the best measure to verify self-report of abstinence, especially when examining short-term treatment outcomes. They also suggested that a less costly, onsite, readily accessible measure of nicotine use, but with greater validity than carbon monoxide, would be a great asset for researchers. One example of this may be the near-patient cotinine test, discussed in the previous section.

1.7.8 Other Biomarkers Used in Smoking Cessation

A number of other biomarkers have been used to determine smoking status. Thiocyanate is one, though it is not so widely used as other biomarkers. If used, it is often combined with other tests such as CO (Hurt *et al.*, 2000), serum cotinine (Seersholm *et al.*, 1999) or both serum cotinine and CO (Waage *et al.*, 1992). As thiocyanate is not a nicotine metabolite, it has been used to determine smoking status in the presence of nicotine, either in the form of nicotine inhalers (Hurt *et al.*, 2000) or to discriminate smokeless tobacco users from cigarette tobacco users (Holiday *et al.*, 1995).

1.7.9 Use of Cotinine in Measurement of Environmental Exposure to Tobacco

Environmental exposure to tobacco is of increasing concern, particularly from a public health perspective. There are issues around children being exposed to passive smoking in the home, particularly if the child is asthmatic. Occupational exposure in public places, such as bars and restaurants, has recently been the focus of attention, and urinary

cotinine has been used to quantify the risks to individuals (Akbar-Khanzadeh, 2003; Johnsson *et al.*, 2003).

1.7.10 Summary

It is now accepted that to measure smoking status, especially in smoking cessation trials, in addition to collecting data by self-report, it is essential to biochemically validate the findings. Carbon monoxide monitoring is the most frequently used means of verifying smoking status due to cost considerations. However, problems with this methodology include its short half-life and lack of specificity. Cotinine measurement provides the most sensitive means of detecting exposure to nicotine and can be measured in blood, urine and saliva. Whilst it is considered the best biomarker for exposure to tobacco smoke, its cost may continue to be a barrier to its more widespread use, except in the area of research.

1.8 Psychological Aspects of Smoking Cessation

Individuals generally do not stop smoking without first deciding that this is a desirable outcome. There are two factors which can give an indication of the likelihood of an individual smoker stopping smoking: **addiction** (compulsive smoking characterised by dependence, both physiological and psychological) and **motivation** (desire/intention to stop smoking) (Foulds, 1996).

1.8.1 Addiction

Tobacco is now considered to be a drug of addiction. Historically, the term drug addiction meant that tolerance developed to the effects of a drug during repetitive use, and that after cessation, withdrawal symptoms emerged (termed physical addiction)

(Benowitz, 1992). A more modern definition regarding addiction is that it can be defined as 'a drug or stimulus which has unreasonably come to control behaviour' (WHO, 1992; American Psychiatric Association, 1995). In essence, the terms addiction and dependence are used interchangeably, in the literature (Tobacco Advisory Group of the Royal College of Physicians, 2000).

There is no doubt that many tobacco smokers become nicotine dependent. However, researchers agree that individual smokers differ in the degree to which they become dependent (Shiffman, 1991). There is good evidence that the degree of dependence is closely related to frequency of smoking (Etter *et al.*, 1999). It would appear that adults who consistently smoke fewer than five cigarettes per day on at least four days per week, over a long period of time are non-dependent. Non-dependent smokers, who are able to increase/decrease their consumption of nicotine are known as 'chippers' (Shiffman, 1989). These smokers report no signs of nicotine withdrawal after overnight abstinence. However, chippers' nicotine absorption per cigarette and nicotine elimination rates have been found to be similar to those of heavy smokers (Shiffman *et al.*, 1992).

It has been suggested that vulnerability to nicotine dependence is related to genetically-based high sensitivity to nicotine (Pomerleau *et al.*, 1993). Consistent with this is the finding that people who become highly dependent smokers have been found to have experienced more pleasurable sensations at their initial exposure to tobacco (Pomerleau *et al.*, 1998).

One feature of addiction is when the substance or stimulus is removed, the individual can suffer from withdrawal symptoms. This leads to a set of signs/symptoms caused by the abstinence of nicotine to which the individual has physiologically adapted. Nicotine withdrawal is now a recognised disease and is included in the *Diagnostic and Statistical Manual of Mental Health Disorders* (DSM – IV) (American Psychiatric Association, 1994).

Nicotine withdrawal can be recognised by patients suffering from at least four of the withdrawal symptoms listed below:

depression or dysphoric mood

irritability, frustration or anger

anxiety, tension

feeling light-headed

restlessness

difficulty in concentrating

insomnia

decreased heart rate

increased appetite or weight gain

urge to smoke

Symptoms usually reach a peak of intensity about 48 hours after smoking cessation and then gradually decline over 3-4 weeks (Hughes and Hatsukami, 1986). Craving and hunger may continue for several months. When smokers quit, even if they don't increase the amount of food they eat, they may put on weight. This is because nicotine is a stimulant which increases the metabolic rate and helps to burn calories.

The single most important element of the withdrawal syndrome is the urge to smoke. It has a direct relationship with failure to quit, and is predictive of subsequent relapse to smoke (West *et al.*, 1996).

1.8.2 Measuring Nicotine Addiction

Nicotine dependence consists of both physical and behavioural components. Most research has addressed the concept of physical addiction. Two widely-used nicotine dependence assessment instruments that determine the extent to which nicotine controls behaviour are the Fagerstrom Test for Nicotine Dependence (FTND) (Heatherton *et al.*, 1991) and its predecessor, the Fagerstrom Tolerance Questionnaire (Fagerstrom, 1978).

A shortened version, used to look at physical dependence, is the Heaviness of Smoking Index. This is a two-question instrument which looks at number of cigarettes per day and time to first cigarette of the day (Kozlowski *et al.*, 1994). These two questions are thought to be the most important in determining tobacco dependence of individuals.

There are other instruments which can be used to measure dependence, such as the screening questionnaire for tobacco dependence according to ICD-10, DSM-III R and DSM IV, as developed by Kawakami and co-workers (Kawakami *et al.*, 1999). These more recently developed instruments are not so widely used as the FTND.

1.8.3 Motivation

A smoker's motivation defined as 'the drive, intention or desire to smoke' is clearly critical in whether the individual succeeds or not in stopping smoking (Foulds, 1999). Smokers differ in their motivation to quit, and these differences are thought to affect likelihood of quitting. There is some merit in assessing level of motivation in smokers with a view to helping those who at the time are more highly motivated, rather than targeting an intervention at those smokers who currently have no intention of stopping smoking (Foulds, 1996).

1.8.4 Measuring Motivation to Quit

There are two commonly used methods of assessing motivation. The first method consists of asking smokers a few simple questions about strength of desire to stop smoking, focusing on how much they want to stop altogether and if they could quit easily, would they do so (Foulds, 1996). A higher score is thought to be predictive of greater likelihood of quitting.

Another method of assessing motivation to change is that implicit in the 'Stage of Change' model of human behaviour. The 'Transtheoretical' Model, advanced by Prochaska and DiClemente (1983), provides a theoretical structure for assessing these changes. This model recognises that smokers go through a series of stages (not necessarily linearly) on the way to achieving non-smoking status. The stages are as follows: *precontemplation*: currently smoking and not seriously considering quitting within the next six months, *contemplation*: currently smoking and seriously considering quitting within the next six months (but not within the next 30 days), *preparation*: currently smoking and seriously intending to quit within the next 30 days, or had a quit attempt of 24 hrs or more in the last year, *action*: not currently smoking, having quit within the last six months, *maintenance*: not currently smoking, having abstained for over six months. It is suggested that progress through the stages is driven by a series of 10 processes, specific to different stages, including consciousness raising (seeking information about the problem behaviour) and stimulus control (controlling situations that may trigger relapse into old behaviour) (Whitelaw *et al.*, 2000).

If smokers relapse, they return to an earlier stage in the model. This model also acknowledges that smoking cessation is often a cyclical activity, rather than one

individual, discrete event and that a smoker may go round the cycle several times before succeeding in quitting (DiClemente *et al.*, 1991). Basic research would indicate that in populations of smokers, 40% are in precontemplation, 40% in contemplation and 20% in the preparation phases (Prochaska and Velicer, 1997).

This method of assessing motivation has been used to predict the likelihood of making an attempt to quit. It can also be used to measure progress through the different stages of change, for those smokers still smoking, but thinking more seriously about quitting.

This model has been used extensively in smoking cessation research in a variety of settings and with different client groups (Bunton *et al.*, 1999).

Some evidence is available which indicates that smokers in the earlier stages are not as successful at quitting as smokers who are in later stages (Prochaska *et al.*, 1993). There is also some evidence that interventions, designed to link with a motivational stage, lead to better outcomes than do non-tailored interventions of equal intensity (Prochaska *et al.*, 1993; Ashworth, 1997).

Though this model is used extensively in the smoking cessation field, a number of researchers are critical of some of its applications (Bunton *et al.*, 2000; Littell and Girvan, 2002). A review, commissioned and published by the Health Education Board for Scotland, outlines some of the methodological problems and limitations of the 'Stage of Change' (Bunton *et al.*, 1999). Around 1000 papers were identified as using or mentioning the model, of which 300 were examined in detail. The largest sub-group

of references were in the field of substance use/misuse including smoking, though other areas such as diet, exercise, sexual and mental health were identified.

In this detailed critique, Bunton and co-workers identified problems both with the internal structure of the model with regard to the descriptors of the stages, and its external validity (its application) in health promotion.

Other researchers raise concerns regarding a lack of consistency regarding the questionnaires used in the different studies (Etter and Sutton, 2002; Littell and Girvan, 2002). Unlike the Fagerstrom Test for Nicotine Dependence where there is one standard research instrument, with 'Stage of Change', researchers often have to design their own and this will lead to lack of standardisation and inconsistency.

Despite the contrasting views of researchers, it cannot be disputed that its widespread use in health promotion, especially with regard to substance misuse, has had an impact, and further evaluation and validation is required to determine its full potential.

1.9 Strategies for Smoking Cessation

1.9.1 Policy Documents including Evidence-Based Guidelines

A number of evidence-based documents have influenced policies with regard to smoking cessation in the UK. In the USA, in the mid 1990's, the Agency for Health Care Policy and Research (AHCPR) released guidelines on treating tobacco dependence (Fiore *et al.*, 1996). These were updated in 2000 (Fiore *et al.*, 2000). The AHCPR guidelines are based on evidence from 300 selected articles which have been extensively reviewed and subjected to meta-analysis. They provided guidance for three

key audiences, primary care clinicians, tobacco cessation specialists and health care administrators.

Other key influences on evidence-based policy are the systematic reviews conducted by the *Cochrane Tobacco Addiction Review Group* in the UK (the Cochrane Library reviews). These reviews present evidence, results and conclusions based on meta-analysis and systematic reviews of randomised clinical trials selected from the literature according to strict inclusion criteria. However, they do not make recommendations.

Both the AHCPR Guidelines and Cochrane Reviews have influenced the development of policy documents in both Scotland and England. In Scotland, the '*Smoking Cessation Guidelines for Scotland*,' were released in 2000, and aimed to set out guidance on the delivery of smoking cessation within the context of the National Health Service (ASH Scotland & Health Education Board for Scotland, 2000). This document was adapted from the English Guidelines, '*Smoking Cessation Guidelines for Health Professionals*' (Raw *et al.*, 1998). The recommendations given in both these documents are targeted at three levels; the primary care team, all health professionals and smoking cessation specialists. Due to rapid changes occurring, especially with regard to health care policy, the English guidelines were updated and republished in 2000 (West *et al.*, 2000). More recently, the Scottish guidelines have also been rewritten and were published in September 2004 (Health Scotland and ASH Scotland, 2004).

Two further Scottish documents, released in 2004, reinforce the current tobacco agenda. These are entitled '*Reducing Smoking Related Harm*' (NHS Health Scotland and ASH Scotland, 2004) and '*A Breath of Fresh Air for Scotland - Tobacco Action Plan*'

(Scottish Executive, 2004a). The former document identifies three areas of priority, namely: a more intensive approach to discourage children and young people from smoking, a marked expansion in smoking cessation services, and the development of further ways to make public and work places smoke-free. The Tobacco Action Plan follows through with an agenda to address these three priority areas.

1.9.2 Community Approaches to Smoking Cessation

The Cochrane Group has undertaken a systematic review of community interventions for reducing smoking among adults (Secker-Walker *et al.*, 2004). The aims were to ascertain whether community-based interventions reduced smoking as measured by prevalence, cigarette consumption and quit rates, when compared to no intervention in comparison communities. It further aimed to detail what characteristics of the studies related to their efficacy. A community intervention was defined as a coordinated multidimensional programme aimed at changing adult smoking behaviour, involving several segments of the community and conducted in a defined geographical area. The size of the communities varied, with the population ranging from a few thousand to over 100,000 people.

The reviewers identified 32 studies for inclusion within the review. Nineteen interventions (59%) aimed at cardiovascular risk factor reduction, with nine (28%) aimed solely at reducing tobacco use. In 20 studies, there was a description of the process of community involvement. A variety of public events, such as lectures or health fairs were used in 28 studies (88%). Mass media was used in 26 studies (81%), 18 (56%) used radio, with 11 (34%) using television spots. Posters/billboards were used in 21 studies (66%). Interventions aimed specifically at smoking included

materials such as quit-kits in 18 (56%) studies, cessation groups in 16 (50%), individual counselling in nine (28%), audiotapes/videotapes in nine (28%) and quitlines in four (12%) of the projects.

Cross-sectional follow-up was used to evaluate the interventions in 14 studies (44%) and cohort follow-up in 10 (31%), and both cohort and cross-sectional follow-up in the remaining eight (25%). Questionnaires were administered in person in 20 studies (63%), by telephone in 13 (41%) by both methods in three and by mail in two. Biochemical testing was obtained in 10 studies (31%), and examples of this included exhaled carbon monoxide and serum or salivary cotinine.

Twenty seven (84%) studies reported differences in smoking prevalence as their main outcome, 14 studies (45%) reported changes in number of cigarettes and 16 studies (50%) reported quit rates.

When looking at the changes in smoking prevalence, the estimated net decline ranged from -1.0% to 3.0% for men and women combined (10 studies). For women, the decline ranged from -0.2% to $+3.5\%$ per year, and for men the decline ranged from 0.4% to $+1.6\%$ per year. In one of the most rigorously conducted studies, the US COMMIT (Community Intervention for Smoking Cessation), there were 11 pairs of US and Canadian communities with a combined population of 2,000,000, which participated in a randomised control trial of a variety of community smoking cessation interventions. This study showed evidence of a limited effect, with no difference in prevalence between intervention and control, and there was no significant difference in the quit rates of heavier smoker, who were the key target intervention group. Dentists

were surveyed within the test areas concerning their tobacco control activities and it was found that, in general, their activities lagged behind those of the physicians, with 48% of the dentists counselling their patients, compared to 94% of the physicians (Jones *et al.*, 1993).

In conclusion, the failure of the largest and best-conducted community-based study to detect an effect on prevalence of smoking is disappointing. Though such approaches will continue to be part of tobacco health promotion policies, future studies will need to take account of this limited effect and consider other options (Secker-Walker *et al.*, 2004).

1.9.3 The 'Stepped Care Approach'

Following its 1996 and 2000 reviews, the US Agency for Health Care Policy and Research (AHCPR) proposed a 'stepped approach' to smoking cessation. This involved the provision of 'brief' low cost interventions for smokers who could stop without extensive support, moving up to the provision of specialist smoking cessation clinics for the most dependent smokers. A similar approach was adopted in Scotland, where the intensity of the intervention was matched to the smokers' level of motivation and addiction (ASH Scotland & Health Education Board for Scotland, 1998). All health professionals were seen to have a role in delivering smoking cessation advice, including general medical practitioners, practice nurses, health visitors, pharmacists, dentists, dental hygienists and health promotion specialists (ASH Scotland & Health Education Board for Scotland, 2000).

Evidence for this multi-professional approach, came from a meta-analysis of 108 interventions used in 39 control trials of smoking cessation in medical practice. It was found that the greatest success was achieved when there were multiple interventions given by multiple health care providers on multiple occasions (Kottke *et al.*, 1988).

The policy recommended that each smoker should be targeted with the least expensive treatment that was likely to enable that person to stop smoking (ASH Scotland & Health Education Board for Scotland, 2000). There were four steps, each of which were appropriate for smokers with particular levels of addiction.

1. The first level of intervention involved the provision of health education and other information designed to increase motivation to quit. This could be delivered relatively cheaply to the population via the mass media.
2. The second level was provision of *very brief* advice (up to three minutes) on stopping smoking by a health professional, including dentists and hygienists.
3. The third level was for healthcare workers to offer nicotine replacement therapy, plus a follow-up appointment. This could take up to 20 minutes of a professional's time.
4. The fourth level involved the provision of intensive treatment in a specialist clinic, for the most highly addicted of smokers. Specialist counselling, group therapy, as well as intensive support including NRT may be used.

1.9.4 Individual Approaches to Smoking Cessation

There are a number of approaches that can be used to give individual advice to smokers (Fiore *et al.*, 1996). Two factors govern the delivery of smoking cessation advice; length of time taken to deliver a clinician-patient interaction, and number of sessions that a patient may receive with respect to smoking cessation advice. The greater the input in time and number of sessions, the higher the success rate (Fiore *et al.*, 2000).

Individual advice can vary from ‘*very brief*’ advice, where attention is drawn to the smoker’s habit, and there is advice given to quit which lasts no more than 3 minutes. The main effect of this advice would be to motivate attempts at quitting, rather than to increase cessation rates (Health Education Board for Scotland and ASH Scotland, 2001). Most of the advice on smoking cessation, delivered in the dental setting will be within the timeframe of this category. With respect to the success rate expected with this type of intervention, it is stated that at 6-months, around 2% of smokers given this type of advice would quit (NHS Health Scotland and ASH Scotland, 2004).

‘*Brief advice*’ to stop smoking may be structured, and can last around 10 minutes. Examples of this approach would include the **4/5As**, and is covered in detail in Section 1.9.5 below. The length of this approach will make it suitable for delivery within a dental setting. The success rate expected with this type of intervention, dependent on whether NRT is used, would be around 5-12% of smokers quitting the tobacco habit (NHS Health Scotland and ASH Scotland, 2004).

More detailed counselling /psychosocial interventions will take a longer period of time, ranging from 10 to 30 minutes to deliver to the patient. Examples of this type of

intervention would include motivational interviewing and its derivatives, 'brief motivational interviewing/behavioural change counselling'. Motivational interviewing is covered briefly in Section 1.9.6 below. As the training required to deliver motivational interviewing is considerable, and the time available in a dental setting for the delivery of smoking cessation advice will be restricted, there is probably limited application for this technique within the general dental practice setting.

1.9.5 'Brief Advice'

Much of the smoking cessation advice in primary care is thought to focus around 'brief advice' which should be provided routinely with some information on NRT and how to use it, and a follow-up visit (Fiore *et al.*, 2000). The method of delivery varies, from flow charts with the essential elements of asking the patient about their smoking and advising them to quit, to more structured protocols which attempt to give the health professional more guidance in delivering such advice (Health Education Board for Scotland and ASH Scotland, 2001).

One such protocol, known as the **4As**, appears in the dental literature (Christen *et al.*, 1990; Chestnutt, 1999). The **4As** are:- **A**sk about smoking at every opportunity, **A**dvice all smokers to stop, **A**ssist the smokers to stop, and **A**rrange follow-up and appropriate referral if required. This structured method of giving advice was used in one smoking cessation trial in general dental practice in the UK (Smith *et al.*, 1998). Trials in other settings, such as general medical practice and in secondary care with pregnant women, have used this approach (Kviz *et al.*, 1995; Melvin *et al.*, 2000).

More recently, the **5As** have been used to help professionals provide smoking cessation advice for their patients (Fiore *et al.*, 2000; Health Education Board for Scotland and ASH Scotland, 2001) This methodology was first outlined for use by physicians, but is suitable for use by all health professionals (DiClemente *et al.*, 1991). In addition to the **4As** as detailed above, the fifth 'A' makes reference to **Assessing** the patient with regards to readiness to quit. This acknowledges that not all patients are ready to quit, and tailors advice on cessation to an individual patient, dependent on the patient's 'Stage of Change'. There have been no trials in the dental field using this particular model of structured smoking cessation advice. The **5As** have been used in general medical practice, particularly in the US and Australia, and with pregnant smokers (Litt, 2002; Solberg *et al.*, 2002; Dept of Health Australia, 2004.)

There is one group where there is no evidence that the use of **5As** is efficacious, and this is with cancer patients (Schnoll *et al.*, 2003). It was concluded that this group required more personalised advice, which reflected and addressed their individual situations.

1.9.6 Motivational Interviewing

Motivational interviewing is a more patient-centred approach for use with helping individuals change their behaviour. Motivational interviewing can be defined as 'a directive, client-centred counselling style for eliciting behaviour change by helping clients explore and resolve ambivalence' (Rollnick and Millar, 1995). Motivational interviewing is influenced by 'Stage of Change' and has self-efficacy and patient-centred counselling as key concepts (Rollnick *et al.*, 1999).

There has been recent interest in the technique, especially when used with pregnant smokers (Tappin *et al.*, 2000; Velasquez *et al.*, 2000).

A systematic review looked at the effectiveness of behavioural interventions, adapting the principles and techniques of motivational interviewing (MI) in the four behavioural domains of substance abuse, smoking, HIV risk and diet/exercise (Dunn *et al.*, 2001). In total, 29 studies were identified and monitored. Sixty per cent of the 29 studies yielded at least one significant behaviour change element. There was evidence that MI can be an effective substance abuse methodology when used by clinicians who are non-specialists, but there was inadequate evidence to evaluate the effect of MI in other domains including smoking.

In a study which aimed to reduce passive smoking exposure in low income households with young children, there was some evidence that the intervention group who had a motivational interviewing session from a trained counsellor and telephone follow-up had lower nicotine levels than those from the self-help group (Emmons *et al.*, 2001).

In another study looking at group counselling for smoking cessation, cognitive/skill training therapy (CBT) and motivational interviewing (MI) therapy were compared with 'brief intervention' (BI) in a sample of 677 smokers (Smith *et al.*, 2001). All participants received 8 weeks of nicotine patch therapy. Neither the MI nor the CBT improved long term abstinence rates relative to the 'brief intervention' (BI).

Motivational interviewing is a relatively new methodology and requires further research and evaluation to examine its future potential in the field of smoking cessation.

1.9.7 Specialist Approaches to Smoking Cessation including Group Therapy

Specialist smoking cessation services are now a key strand in the provision of smoking cessation. It is to these services that those individuals who are most heavily dependent on tobacco should be referred for treatment. Usually, a specialist smoking cessation clinic will offer individual counselling as well as group therapy, dependent on a client's individual preference. The individual will also be encouraged to use nicotine replacement therapy (NRT) if required.

Both Scottish and English smoking cessation services use group counselling which focuses on group processes rather than the therapists educational or counselling input (Hajek and West, 1998). This withdrawal-orientated therapy is based on the premise that smokers fail because of the severity of withdrawal symptoms, and if one can address this problem, the likelihood of success is higher (Hajek, 1989). This treatment methodology has been pioneered at the Maudsley Clinic in London. Participants are registered with a view to attending weekly for six weeks, where they meet and receive professional advice, as well as social support from each other.

Since 1998, England has developed smoking cessation services in all of its regions, following the release of the White Paper *'Tobacco Kills'* (Department of Health, 1998). Evaluation of the specialist smoking cessation clinics in England has resulted in extremely encouraging results (Department of Health, 2003). Figures released for specialist services, April 2001-March 2002, indicated that 227,300 users had set a quit date and of those, about 142,300 (63% of those setting a quit date) received free NRT. At the 4-week follow-up, 119,800 (53%) said that they had quit (self-report). This is considerably in excess of success rates associated with the 'brief intervention', though

direct comparison is difficult, as results of other smoking cessation studies often report quit rates at 3 and 6 months, rather than at 1 month.

With respect to the Scottish Specialist Smoking Cessation Services, these have been developed more recently, and what is available varies geographically. Greater Glasgow, for example, runs mainly group counselling sessions, whereas Tayside offers only individual counselling. Currently, no evaluation figures are available for Scottish specialist smoking cessation services. *Partnership in Action on Tobacco and Health* (PATH), part of ASH Scotland, are currently developing data collection tools to be used in the evaluation of all Scottish Cessation Services.

1.10 Therapeutic Aids to Smoking Cessation

1.10.1 Nicotine Replacement Therapy

Nicotine Replacement Therapy (NRT) is used to replace the nicotine from cigarettes in smokers who wish to quit smoking. This reduces the withdrawal symptoms associated with smoking cessation (Royal College of Nursing, 2001). It minimizes many of the physiological and psychomotor withdrawal symptoms, and therefore its use increases the likelihood of motivated smokers quitting and remaining abstinent (Hughes *et al.*, 1990). All forms of NRT use routes of absorption other than gastric, as nicotine is rapidly broken down in the acidic environment of the stomach (Tang *et al.*, 1994).

A Cochrane Review provides evidence, from over 35,600 smokers, that offering NRT products to dependent smokers is more effective in helping them stop smoking than if NRT is not offered or if a placebo is used (Silagy *et al.*, 2004). The review identifies 110 trials of which 96 were associated with a non-NRT control group. The main

outcome measure was abstinence from smoking after at least six months of follow-up. The odds ratio for abstinence with NRT compared to control was 1.74 (95% confidence interval, 1.64-1.86). The odds ratios for the different forms of NRT were 1.66 for gum, 1.74 for patches, 2.27 for nasal spray, 2.08 for inhaled nicotine and 2.08 for nicotine sublingual tablet. The odds were largely independent of the duration of the therapy, intensity of additional support provided or the setting in which the NRT was used.

1.10.2 Nicotine Gum

The first type of NRT to be developed was chewing gum in 1967 (Royal College of Nursing, 2001). This was prompted by a request from the Swedish Navy to a pharmaceutical firm regarding the problems they had with their submarine crews suffering from nicotine withdrawal, when they were on board ship.

The nicotine resin complex is presented in a buffered chewing gum base which enables the nicotine to be absorbed directly through the buccal mucosa resulting in plasma concentrations approximately half that produced by smoking a cigarette (Russell *et al.*, 1976).

Nicotine gum was first launched in the UK as a prescription-only 2 mg gum, followed thereafter by a 4 mg gum for use with more highly dependent smokers. Currently, both formulations are available on the general list and can be bought in supermarkets in a similar manner to toothpaste or sugar-free gum.

The first randomised controlled trial (RCT) trial of nicotine gum was carried out in the early 1980s (Jarvis *et al.*, 1982). One hundred and sixteen subjects who were smoking

between 26 and 30 cigarettes a day were recruited, and told to use unrestricted amounts of the 2 mg gum. Of the 58 participants who received the nicotine gum, 27 (47%) were not smoking at 1 year, compared to 12 (21%) of the placebo gum users.

In a recent trial, 608 smokers were characterised into high and low nicotine dependence (Garvey *et al.*, 2000). Subjects were assigned to placebo, 2 mg or 4 mg nicotine gum groups. Brief behavioural counselling was also used. At 1 year, post-cessation quit rates were 11.2%, 19.5% and 18% for the low dependence group using placebo, 2 mg and 4 mg gum respectively. For the more highly nicotine dependent group, quit rates were 6.1%, 15.7% and 20.7% for placebo, 2 mg and 4 mg gum respectively. Other variables relating to quit rate at one year were longer period of abstinence on a prior quit attempt, being married, higher educational status and having a non-smoking partner.

Side effects of gum can include hiccups, gastrointestinal upset, jaw pain and orodental problems (Palmer *et al.*, 1992).

1.10.3 Nicotine Patches

The nicotine patch consists of a self-adhesive transdermal delivery system (Royal College of Nursing, 2001). Two types of patch are available: a 24 hour patch designed to be worn day and night, and a 16 hour patch which is applied first thing in the morning and removed at bed time. There is no difference in efficacy between these dosage regimes (Silagy *et al.*, 2004).

The patch works by slowly releasing a controlled amount of nicotine over a 16 or 24 hour period, i.e. all the time it is worn. Properties of nicotine make it ideal for

transdermal delivery. Being lipophilic, it can permeate through the stratum corneum, and its hydrophilic properties also mean it can pass through the deeper layers of skin and reach the systemic circulation. This produces lower levels of nicotine than smoking, but high enough to prevent withdrawal symptoms such as irritability, restlessness and anxiety.

Nicotine patches were first launched in the UK in 1992. In a study of 1200 heavy smokers (defined as >15 cigarettes per day) attending general medical practice, participants received 'brief' GP advice, a booklet and 16hrs/day patches, either active or placebo (Stapleton *et al.*, 1995). Outcomes were measured at follow-ups at weeks 1, 3, 6, 12, 26 and 52 by self-report and biochemical validation. It was found that nicotine patch treatment doubled the rate of continuous abstinence, up to one year.

1.10.4 Other Forms of Nicotine Delivery

There are other forms of nicotine delivery, namely lozenges, tablets, inhalator and nasal spray (Royal College of Nursing, 2001). Choice of product is often dependent on the preference of the individual making the quit attempt. Nasal sprays may be more suitable for those who are more highly dependent, as they have the most rapid nicotine delivery system of all the nicotine replacement therapies.

One study, in which smokers were randomised to nicotine gum, patch, spray or inhaler found no significant differences in abstinence rates after 12 weeks (Hajek *et al.*, 1999).

1.10.5 Combination of NRT therapy

There is some evidence that using a combination of NRT products is better than one product alone (Silagy *et al.*, 2004). For those patients unable to quit on a single type of NRT, updated US Clinical Practice guidelines recommend use of nicotine patches with another form of NRT as a second-line therapy, or with bupropion (Fiore *et al.*, 2000). Currently, NRT products are not licensed for use in this way in the UK.

1.10.6 Non-Nicotinic Preparations used in Smoking Cessation

1.10.6.1 Zyban (Bupropion)

Sustained-release bupropion (amfebutamone) is a non-nicotinic agent that is indicated as an aid to smoking cessation. Its smoking cessation properties were discovered when it was noted that some smokers, using the drug for antidepressant reasons, quit smoking. Its mechanism of action in smoking cessation is not fully understood, but it may be mediated by raising the concentration of dopamine in the brain (Ascher *et al.*, 1995).

In two large clinical trials, use of bupropion (300mg/day) for 7-9 weeks, was associated with significantly higher smoking abstinence rates than placebo at 6 and 12 month follow-ups (Hurt *et al.*, 1997; Jorenby *et al.*, 1999). Point prevalence rates at 12 months in the two studies were 23.1% and 30.3% with bupropion, compared to 12.4% and 15.6% for the placebo. Continuous abstinence rates at 12 months in the second trial were 18.4% with bupropion and 5.6% with placebo (Jorenby *et al.*, 1999). However, some side-effects were noted, and insomnia and dry mouth were reported by a number of the patients. A seizure rate of 0.1% of patients using this drug has been reported (Hurt *et al.*, 1997).

When looking at the efficacy of bupropion and NRT patch, versus placebo and NRT patch, it was found that the combination therapy of bupropion and nicotine patch provided a slightly higher abstinence rates than NRT alone (Jorenby *et al.*, 1999).

1.10.6.2 Other Drugs Used in Smoking Cessation

Other drugs such as nortriptyline and clonidine have been used in smoking cessation (Tobacco Advisory Group of the Royal College of Physicians, 2000). Further research is required to investigate their full potential.

1.11 Involvement of Primary and Secondary Health Care in Smoking Cessation

1.11.1 Smoking Cessation Advice Delivered by Physicians

A vast amount of information is available concerning the delivery of smoking cessation advice by a medical practitioner and a systematic review, using Cochrane methodology, has been carried out (Silagy and Stead, 2004).

Selection criteria included the use of randomized controlled trials with at least two groups and assessment of abstinence, at least 6 months after the advice was given.

This review did not look at the effect of adding NRT to advice, as the effectiveness of this was addressed in a separate Cochrane review.

The review had as its primary objective, to determine whether giving advice was more effective than not giving advice and whether the effect was greater if the advice was more intense and followed-up. The review also examined the effect of supplementation of advice with various aids such as self-help manuals and CO monitoring and looked at

whether motivational interviewing was more effective than simple advice. Studies where advice was provided (with or without a leaflet) during a consultation lasting less than 20 min and with up to one follow-up visit was defined as a 'minimal' intervention. Any trial where the intervention involved a greater time commitment at the initial consultation, or used additional materials was defined as an 'intensive intervention'.

The Cochrane review identified 34 trials, conducted between 1972 and 1999 and including over 27,000 smokers, which met the criteria. Some of the populations were at risk of specific diseases, including asthma, ischaemic heart disease and diabetes. Most trials were set in primary care, though other settings included hospital wards and outpatient clinics.

The primary outcome measure was that of smoking cessation, rather than smoking reduction. Validation of all self-reported cessation by biochemical analysis of body fluids or measurement of CO was reported in nine of the studies (26%). No biochemical validation was reported in the remaining 21 studies (62%). It is rather surprising that the number of studies using validation was so low.

When all 16 trials of brief advice (as part of a minimal intervention) versus no advice (or usual care) were pooled, the results demonstrated a statistically significant increase in the odds of quitting [OR 1.69, 95% CI 1.45-1.98]. When the effectiveness of more intensive advice was compared to no advice/control, there was a trend towards a larger effect, but there was evidence of heterogeneity between the trials. A direct comparison between intensive and minimal advice in 15 trials suggested a small but significant advantage of more intense advice.

Even though motivational interviewing appeared to increase the likelihood of making a quit attempt, a single trial produced insufficient evidence to support the benefit of motivational counselling compared to brief advice on cessation rates (Butler *et al.*, 1999).

1.11.2 Smoking Cessation Advice Delivered by Nurse Practitioners

A further Cochrane review looked at nursing interventions for smoking cessation (Rice and Stead, 2004). The aim of this review was to determine the effectiveness of nursing-delivered smoking cessation interventions, in comparison to no intervention. Additional areas examined were the intensity of the intervention, and whether the intervention was more effective if it included follow-up or other aids to smoking cessation.

Criteria for inclusion were that there had to be at least two treatment groups and allocation to treatment groups had to be stated as random. Types of participant were adults of either gender, but specifically excluding pregnant women (this is the subject of a separate Cochrane review). Follow-up of patients had to be at least to 6-months.

Advice to stop smoking was defined as verbal instructions from the nurse to stop smoking. Low intensity interventions were defined as trials where advice was provided (with or without leaflet) during a single consultation lasting 10 min or less, (half the time used in the physician review), with up to one follow-up visit. High intensity interventions were defined as trials where the initial contact lasted for more than 10 min, or where there were additional materials or strategies other than simple leaflets and participants usually had more than one follow-up contact. As with the physician review, studies using NRT were specifically excluded.

Outcome measures were smoking cessation or reduction in the number of cigarettes smoked. Where biochemical validation was used, only those subjects meeting the biochemical criteria were regarded as quitters.

The reviewers identified 22 trials between 1987 and 2000 in seven different countries. Twenty trials recruited hospitalised patients or primary care patients and two studies used community-based adults. Eight studies focussed on adults diagnosed with cardiovascular problems, one study each with patients with diabetes or respiratory disease.

Sixteen studies, involving 8192 people, contributed to the main comparison of nursing advice versus control. In these 16 studies, comparing a nursing intervention to a control or usual-care group, it was found that allocation to the intervention significantly increased the odds of quitting [OR 1.50 95% CI 1.29-1.73]. There was no evidence from indirect comparison that interventions classified as more intensive were more effective than less intensive ones. There was limited evidence that interventions were more successful for hospital inpatients with cardiovascular disease than for other conditions. Interventions in non-hospitalised patients also showed evidence of benefit. Five studies, not included in the main analysis, involving nurses giving smoking cessation counselling during a screening health check, showed some, albeit a lesser, effect.

1.11.3 Smoking Cessation Advice Delivered by Community Pharmacists

For a variety of reasons, community pharmacists are increasingly being seen as an important group to promote smoking cessation. They have contact with smokers on a day-to-day basis and are the key interface for the distribution of nicotine replacement therapy.

No Cochrane review data are currently available for this group. A protocol has been developed and the completed review is due to be published later in 2004. However, a recent review of the pharmacists' role in reducing the risk factors in coronary heart disease included smoking (Blenkinsopp *et al.*, 2003).

Two RCTs, one in Scotland and one in Northern Ireland/London were identified, together with three non-randomised experimental studies (Sweden, Germany and Switzerland).

The Scottish RCT involved 492 subjects and 62 community pharmacists. At 9 months, 12% of the intervention and 7% of the controls had reportedly quit. Surprisingly, for a more recent study, self-reported quitters were not biochemically validated, the authors stating that they found doing this untenable.

In contrast, the NI/London trial did use validation, in the form of cotinine, to determine smoking cessation. This study involved 484 subjects, with 124 community pharmacists taking part. However, only 44% of these managed to recruit patients into the study. At 1 year, 14.3% of the intervention group were abstinent, compared to 2.7% of the controls.

1.12 Involvement of the Dental Team in Smoking Cessation

With respect to guidance for the dental team regarding the delivery of smoking cessation advice, a number of resources have been developed which focus purely on this topic (Watt and Robinson, 1999; Beaglehole and Watt, 2004). One guide includes smoking cessation advice under the auspices of oral cancer prevention (Macpherson *et al.*, 2003).

With regards to the role of the dental team in smoking cessation, this topic has not been the subject of a Cochrane review, and no other systematic reviews cover this subject area.

This section will therefore review interventions concerning the delivery of smoking cessation advice by primary and secondary care dental team members.

The majority of the available literature examines dental professionals' attitudes and practices regarding the provision of smoking cessation advice. Some papers address issues to do with training received by dental team members or the perceived need for training by dentists and hygienists. A smaller body of literature assesses smoking cessation rates/reduction in cohorts of dental patients recruited to trials. Two papers examine the patients' perspective regarding the involvement of the dental team in promoting smoking cessation.

1.12.1 Dentists and Dental Hygienists Attitudes to Promoting Smoking Cessation

Surveys of dentists concerning their attitudes to promoting smoking cessation have been carried out in the US, UK, Canada, Sweden, Finland, Italy, Germany, the Netherlands, Jordan, Australia and New Zealand, over the last two decades. Some studies in the UK and US surveyed similar groups of dentists 5 years apart, enabling secular trends to be examined with regards to smoking cessation activity (Logan *et al.*, 1992; John *et al.*, 2003). With respect to dental hygienists, surveys have been carried out in the US, Canada, UK and Italy.

The size of the surveys vary, from several thousand questionnaires in some of the US and one UK study, to around one hundred in some of the smaller research projects. Response rates also differ, with some researchers obtaining responses of at least 70% (Telivuo *et al.*, 1991; Logan *et al.*, 1992; Chestnutt and Binnie, 1995) while others obtained response rates as low as 12% (Warnakulasuriya and Johnson, 1999; Reichart *et al.*, 2000). The quality of the responses therefore may vary, depending on the project methodology. Some surveys, despite having a large number of questionnaires, may still have a low overall response rate, and issues to do with bias and selectivity have to be borne in mind.

The surveys also differ in the approaches taken, with some asking about smoking cessation under the banner of oral cancer prevention. However, there are a number of recurring themes.

1.12.2 Dentists' and Dental Hygienists' Roles and Current Practices with respect to Smoking Cessation

One of the main areas examined has been whether dental health professionals consider themselves to have a role in smoking cessation. Most surveys would indicate that high numbers are of the opinion that dentists and dental hygienists should participate in this area, albeit under the auspices of oral cancer prevention.

In the UK (Scotland), Chestnutt and Binnie (1995) found that 55% of dentists said that they had a role in promoting smoking cessation. Other surveys asking comparable questions found slightly higher results in the region of 70% (Campbell and Macdonald, 1994; Warnakulasuriya and Johnson, 1999). With respect to the dental hygienists, there were similar findings in the region of 60-80% of hygienists feeling that they had a role in this area (Fried and Rubenstein, 1990; Gussy *et al.*, 1996; Syme *et al.*, 2001).

By contrast, in one of the most recent studies, carried out in Sweden, half the dentists (49%) and around a third of the hygienists did not perceive that assisting people with tobacco cessation was part of their job (Helgason *et al.*, 2003).

Differing categories of dentists have varying perceptions of their role in tobacco counselling. One group, where advice is most often offered, is the category of periodontist, and this is likely to be due to the role that tobacco plays in the aetiology, prevalence and response to treatment of periodontal disease (Dolan *et al.*, 1997).

The attitudes of paediatric dentists to tobacco intervention work with children and adolescents have been studied, and though high numbers thought they had a role, half (48%) did not feel confident in undertaking this work (Shenkin, 2003).

Some surveys asked the dental health professionals about their own smoking habits. The prevalence of smoking amongst dentists varied from continent to continent. A relatively high number of dentists in Northern Italy and Jordan smoked, with around one in three (33% and 35% respectively) reporting being current smokers (Lodi *et al.*, 1997; Burgan, 2003). This is high compared to rates of Scottish (12%), English (9%), Swedish (16%), American (6%) and Canadian dentists (4%) (Logan *et al.*, 1992; Campbell and Macdonald, 1994; Chestnutt and Binnie, 1995; Halling *et al.*, 1995; John *et al.*, 1997). The reported prevalence of tobacco use by dental hygienists was 7% in both the UK and US (Fried and Rubenstein, 1990; Gussy *et al.*, 1996).

1.12.3 Asking Patients about Tobacco Use

On examining whether the dentists **Asked** their patients about their smoking status, studies often differentiated between asking all or most of their patients, or asking some of their patients.

High numbers of dentists ask at least some of their patients about their smoking status: 90% in the US (Logan *et al.* 1992; Dolan *et al.*, 1997), 80% in Canada (Campbell and Macdonald, 1994), 85% in Scotland and England (Chestnutt and Binnie, 1995; John *et al.*, 2003). Lower numbers of dentists report routinely or always asking about smoking. In England, 48% routinely recorded their patients' smoking status, with 27% always discussing smoking with their patients (John *et al.*, 2003). Comparable figures are 19% in Scotland (McCann *et al.*, 2000) and 33% in the US (Dolan *et al.*, 1997). In Northern Ireland, only 14% of the dentists said that their patients' records routinely contained information about smoking habits (Cowan *et al.*, 1995).

If there were signs or symptoms of oral disease, such as potentially malignant lesions or periodontal disease, dentists felt happier about raising the issue of smoking (John *et al.*, 1997; Clover *et al.*, 1999).

With respect to dental hygienists, Halling *et al.* (1995) found that 68% of hygienists in Sweden routinely took a tobacco history compared to 32% of the dentists. A recently published survey of Italian dental hygienists found that 94% reported asking about patients' tobacco use (Nicotera *et al.*, 2004).

1.12.4 Advising Patients about Tobacco Use

Few dentists always advise their smoking patients to quit, with a larger number advising at least some of their patients to quit. Several studies found around 60% of dentists were likely to advise at least some of their patients to quit (Logan *et al.*, 1992; Dolan *et al.*, 1997).

With respect to dental hygienists, a similar or slightly higher number were likely to routinely advise their patients to quit, with 60% of Iowa hygienists routinely, and 67% of Eastern US hygienists almost always or often advising patients to quit (Fried and Rubenstein, 1990; Chambers and Corbin, 1996).

As with asking patients about tobacco use, a number of studies have reported that dentists find it easier to advise their patients if there is dental pathology present (John *et al.*, 2003). In addition, Martin and co-workers (1996) reported that dentists were more likely to advise patients who smoked heavily (2 packs a day) than smokers who smoked more lightly (a pack or less per day). With respect to dental hygienists, Parker (2003)

postulated that the reason that dental hygienists found it easier to advise patients to quit smokeless tobacco was due to the high prevalence of intraoral lesions in such patients.

1.12.5 Assisting Patients with Smoking Cessation

The literature shows that dentists and hygienists are much less likely to actively assist their patients in trying to quit, than they are to ask and advise on smoking matters (Warnakulasuriya, 2002).

Practitioners have been asked whether they helped patients to set a quit date, whether they gave information about nicotine replacement therapy and whether they referred patients in need to specialist services. Clover and co-workers (1999) in her Australian study found that only 5% of the dentists surveyed helped their patients set a quit date. In a recent Canadian study, less than 10% of dentists provided any method of assistance, such as resources, quit date or referral, for most patients interested in quitting (Brothwell and Armstrong, 2004). In the US, Dolan and co-workers (1997) found that periodontists were the category of dentist most likely to give their patients help in this area.

With respect to dental hygienists, this group were more likely to be proactive than the average dentist, with 24-27% of US hygienists discussing specific strategies to stop smoking with patients (Hastreiter *et al.*, 1994; Chambers and Corbin, 1996).

It has been suggested that even where dentists were willing to participate in smoking cessation, their activities were not systematic and there was a need for further education and training (Wood *et al.*, 1997).

1.12.6 Issues associated with Competency and Perceived Training Need

Many of the studies outlined above asked practitioners to rate their levels of confidence and competence in delivering smoking cessation advice. In many studies, practitioners expressed a need for further training (Chestnutt and Binnie, 1995, Warnakulasuriya, 2002; John *et al.*, 2003).

Within the US, one study reported only 24% of dentists (Texas-Mexico Border) felt adequately trained to provide tobacco cessation education (Alonge and Narendran, 2003), while another showed that less than 10% reported a good knowledge of NRT or Bupropion (John *et al.*, 2003). Block and co-workers (1999) found that 60% of dentists reported a desire for further tobacco education.

With respect to dental hygienists, the concerns cited were similar to those of the dentists, with low confidence in the training already received, especially in the UK (Gussy *et al.*, 1996; Dykes *et al.*, 2001).

A number of surveys have looked at the state of tobacco education in the undergraduate curriculum and found it to be insufficient (Chestnutt and Binnie, 1996; Dykes *et al.*, 2001; Rikard-Bell *et al.*, 2003a). These studies suggest that further structured training at undergraduate level for both dentists and hygienists is essential.

Gelskey (2002) detailed a systematic training approach to tobacco education involving 6 hours of training, which would be suitable for dental health professionals.

1.12.7 Barriers to Participating in Delivering Smoking Cessation Advice

A number of barriers to participating in smoking cessation have been cited by dental health professionals. Lack of confidence, limited resources, doubt about their effectiveness and skills in assisting patients in making a quit attempt, not knowing referral routes for detailed counselling and lack of patient materials were recurring themes in the different surveys (Chestnutt and Binnie, 1995; Warnakulasuriya, 2002; John *et al.*, 2003). Lack of time was mentioned by several studies (Chestnutt and Binnie, 1995; Albert *et al.*, 2002; Watt *et al.*, 2004) and hygienists voiced similar concerns with respect to the barriers mentioned above (Chambers and Corbin, 1996; Gussy *et al.*, 1996). McCann *et al.* (2000) cited fear of adversely affecting the dentist-patient relationship. Lack of remuneration for this work was also mentioned in some studies (Chestnutt and Binnie, 1995; John *et al.*, 1997) though others reported that this was not a strong barrier (Chambers and Corbin, 1996; Dolan *et al.*, 1997).

1.12.8 Patients' Perceptions of Smoking Cessation as delivered by Dental Team

Members

In the UK, there is no research into patients' opinions and attitudes regarding smoking cessation therapy in a dental setting. One Canadian and one Australian study address this topic area.

In rural areas of Alberta, Canada, staff in 52 dental offices were recruited and provided demographic and professional information about their tobacco counselling practices as well as information about their views regarding the patients' opinions of providing such a service (Campbell *et al.*, 1999). Additionally, a random sample of patients, seen during one month at these dental offices, were interviewed over the telephone about their last dental visit. In all, data were collected from 3,088 dental patients of whom

58.5% believed that the dental team should provide tobacco cessation services. This was in contrast to the data collected from the dentists: 61.5% did not think that patients expected such services, and dentists cited patient resistance (94.3%), the fact that patients might leave their practices (53.9%), and lack of confidence in practitioners' ability to provide effective services (90.4%) as barriers.

A more recent study (Rikard-Bell *et al.*, 2003b) looked at Australian patients' views of the counselling they received from their dentist in the field of smoking cessation. Seventy-eight dental practices agreed to allow patients to be approached to collect data. A total of 2,451 patients were contacted, of which 1,160 agreed to participate and to fill in pre-consultation questionnaires. Of this group, 302 (26%) were current smokers. Most patients who smoked reported that they would not change their dentist if asked about their smoking status at every opportunity (61%). Within this group, nearly half of all smoking patients were not seriously intending to quit (46%) and only 79 (26%) were considering quitting. Less than one third of smokers (30%) surveyed stated that they would try to quit if their dentist suggested that they should try.

Patients were also asked to complete questionnaires after their dental consultation. Of the 849 who agreed, 623 returned the postal questionnaires. Of this cohort, only 17% recalled being asked about their smoking status at their most recent visit. With regards to smokers, only 35% recalled any type of smoking cessation advice being given.

Though this was an interesting approach to what amounts to an audit of the delivery of smoking cessation advice, a number of flaws in the methodological approach may be inherent, resulting in potential bias. Only 58% of dentists agreed to allow patients to be

approached, and only 623 (out of a possible 2,451 patients initially approached) completed post-consultation questionnaires. The authors also state that smokers were significantly more likely not to return the post-consultation questionnaires.

1.12.9 Clinical Trials involving Dentists and Smoking Cessation

In the US and UK, dentists have been involved in a limited number of smoking cessation trials and are recognised increasingly as having a small but significant impact upon cessation rates (Gordon and Severson, 2001; Warnakulasuriya, 2002). Two US and two UK trials are discussed below.

In a randomised control trial, Cohen (1997) found that by attaching stickers to the front of the casenotes of patients who smoked, a doubling occurred in the percentage of smokers (36% v 18%) who were asked about their smoking by the clinician.

In previous work, Cohen carried out a randomised control trial involving private dentists in the US (Cohen *et al.*, 1989). Each of the 50 dentists recruited was assigned to one of four experimental legs: 'reminder' group where two prompts on patients' notes reminded the clinician to ask about smoking and to set a quit date; 'gum' group where patients were offered free nicotine gum; 'both' group where patients had both information and free nicotine gum; and a 'control' group who received neither information nor gum. Smoking cessation outcomes were determined at 6 and 12 months, with biochemical validation of smoking status available for 428 participants at 6 months and 374 at 12 months. At 6-months, those patients in the 'gum' leg had a cessation rate of 18.2%, compared with 7.1 and 7.4% for the 'control' and 'reminder' groups. Those patients in the 'both' group had a quit rate of 9.4%. At the 12-month

mark, the rates of quitting for the 'gum' group had fallen slightly to 16.3%, whereas the patients who received 'both' had a success rate of 16.9%. The 'control' and 'reminder' groups had a rate of 7.7% and 8.6% respectively. Despite this trial being around fifteen years old, there is little recently published literature involving the use of NRT in a dental setting. Christen and Christen (1992) described how NRT in the form of nicotine patches could be used within the oral care setting, but no data were presented regarding their effectiveness of such an approach.

In the UK, there have only been two clinical trials reported involving dental team members and the provision of smoking cessation advice. The first study took place in a hospital periodontal department. A group of 98 smokers were given smoking reduction advice, combined with dental health instruction and periodontal care, delivered by one periodontist (Macgregor, 1996). A control group of 33 individuals were given dental health instruction and periodontal care, but no smoking cessation advice. Follow-ups of patients varied, between 3 and 12 months. In the intervention group, 50% reported reducing their consumption of cigarettes to half or less, and 13.3% reported giving up smoking completely. In the control group, 29% reported some reduction in their smoking, with 5.3% of the participants giving up completely. No details were presented regarding the nature of the smoking cessation advice, nor was there any biochemical validation of the smoking status of the patients, with all data regarding giving up smoking or cutting down being self-reported.

In the first UK trial of smoking cessation in a general dental practice setting, Smith and co-workers (1998) found a smoking cessation rate of 11% at 9 months. This study did not have a control phase and there were difficulties associated with recruitment of

patients in some of the practices. Though 54 practices agreed to participate in the study, only 22 (41%) took part, with two practices managing to recruit over one-third of all the patients. A total of 159 patients were recruited to the study. Patients were given counselling based on the 'brief' intervention from the dentists, and they were also offered NRT (nicotine patches at cost price) if they so wished. Smoking status was biochemically validated at baseline and at 9 months using cotinine. Seventeen (out of a total of 159) had stopped smoking at the 9-month mark, and of these seven attributed their success to the help and advice given by the dental team, with ten patients attributing their success to the use of nicotine patches. The main criticism regarding this study was the lack of an RCT design. Other areas of concern include the lack of quality control regarding the actual nature of the smoking cessation intervention, nor was there any formal training of the dental team members involved.

1.12.10 Trials involving Smoking Cessation and Dental Hygienists

There have been a number of tobacco cessation trials reported involving dental hygienists giving advice to smokeless tobacco users; in general these have not been reported in this thesis as they are outwith the area of this study.

No UK trials have been reported involving the use of dental hygienists to give smoking cessation advice to patients. Two US trials, carried out during the 1980's and 90's, have involved dental hygienist-delivered smoking cessation advice.

The first US trial was carried out by Secker-Walker *et al.* (1988). Dental hygienists were trained to deliver the smoking cessation intervention during routine care. The intervention consisted of providing 'brief counselling', self-help material and direct

advice to quit. A total of 51 smokers were recruited. A telephone follow-up questionnaire, administered 6 months after counselling, revealed that 14.6% of the counselled patients quit smoking. Data were collected by self-report and there was neither biochemical validation nor a control group within this trial. The authors state that the best predictors of quitting smoking included an initial high intention of quitting soon, fewer pack-years of smoking and two or more visits to the dental hygienist. Clearly, methodologically, any future trials would have to be more robust, with an RCT design, and quitting validated by some form of biochemical means such as cotinine or CO.

A randomised clinical trial to test a brief intervention in fee-for-service practices was carried out in Oregon (Severson *et al.*, 1998). This intervention principally used dental hygienists. The intervention was targeted at both smokeless tobacco users as well as cigarette smokers. This was the largest trial to date, involving dental team members, and data were available for 3,068 cigarette smokers and 469 smokeless tobacco users recruited into the trial and followed-up at both 3- and 12-months post-intervention.

For the cigarette smoker, three types of intervention were used: 'Usual Care', 'Minimal Intervention' and 'Extended Intervention'. For smokeless tobacco users, two groups were used: 'Usual Care' and 'Extended Intervention'. Minimal Intervention in this trial was defined as, asking about their patients' smoking habits, giving feedback to the patients regarding any smoking-related oral conditions, giving advice to quit and some resources for the patient including a pack of educational materials. The 'Extended Intervention' was defined as all of the above and in addition, setting a quit date with the

patient, giving a motivational video and telephone follow-up regarding the patient's progress.

Two types of outcome measures were used for the cigarette smokers: absolute quit rate and secondary measures looking at quit attempts. The percentages of trial participants who quit at 3-months were 5.1% and 5.6% for Minimal and Extended interventions respectively, with the Usual Care (control group) having a success rate of 4.7%. At the 12-month mark, there was little difference between the groups with the percentages for Minimal, Extended and Usual Care (control) being 2.5%, 2.6% and 2.4% respectively. Secondary outcomes looked at 'readiness to quit', having attempted to quit in the previous 12 months and thinking about quitting in the next 30 days. Those in the Extended Intervention group were significantly more likely to have tried to quit in the last 12 months and to be thinking of quitting in the next 30 days, than either the Minimal Intervention or Usual Care groups.

With regards to the smokeless tobacco intervention, the results were more encouraging: 17.8% of the users had quit at 3 months with the levels falling to 10.4% at 12 months. The authors felt that smokeless tobacco users were more successful in quitting because they may not have been subjected to the same barrage of health messages and environmental restrictions as cigarette smokers and were more receptive to the whole concept.

Problems with this study include no biochemical validation of the smokers' self-reported quitting, and the units of randomisation were also the practices, rather than the patients.

1.12.11 Summary

Whilst a relatively large number of studies have investigated dental team members' views regarding their involvement with smoking cessation activity, very few smoking cessation trials have been undertaken in the dental setting. Methodological concerns are associated with most of these trials, suggesting that further work in this area, using a randomised controlled trial design and appropriate validation of smoking status, is required.

Chapter 2

The Validation of Self-Reported Smoking Status by Analysing Cotinine Levels in Stimulated and Unstimulated Saliva, Serum and Urine

2.1 Introduction

As outlined in the previous chapter, when assessing the effectiveness of smoking cessation interventions, there is increasing emphasis being placed on the use of biochemical validation as a means of determining those individuals who have stopped smoking, and to weed out ‘deceivers’, ie those individuals who self-report that they are non-smokers, but whose biochemistry would indicate that they are still smoking (Gariti *et al.*, 2002).

As detailed in Chapter 1, the biochemical marker used increasingly to determine exposure to nicotine is cotinine. This nicotine metabolite can be used for determining exposure to tobacco via various biological fluids including blood, saliva, cervical exudate, semen and urine (Etzel, 1990; Vine *et al.*, 1993; Poppe *et al.*, 1995). In addition to using cotinine as a means of biochemical verification of a patient’s self-reported smoking status, it can also be used to assess a non-smoker’s exposure to environmental tobacco smoke (Cummings *et al.*, 1990).

The following sections discuss measurement of cotinine in saliva, serum and urine, those fluids most often used in smoking cessation trials.

2.2 Use of Saliva

The main advantage of using saliva is that it is non-invasive to collect, easily accessible and requires no facilities for its collection. Cotinine has been shown to be stable in saliva, thus samples can be sent by post, enabling its use in outreach settings such as dental practices (Greeley *et al.*, 1992). Samples are also able to be frozen with no detriment to the cotinine analysis (Foulds *et al.*, 1994).

Some minor disadvantages of saliva are that it can be more difficult to work with than other sample types in the laboratory, as food intake can affect its consistency and appearance. Saliva also contains non-food particulate matter, such as oral squames and mucopolysaccharides which can contribute to its stringy or sticky consistency (Schramm *et al.*, 1992; Bernert *et al.*, 2000). Salivary collection can sometimes be difficult for those subjects who suffer from 'dry mouth', either idiopathic or drug-induced. Additionally, Trudgill and co-workers found that increasing daily cigarette consumption was associated with lower salivary bicarbonate concentration and a reduced salivary flow rate (Trudgill *et al.*, 1998).

There are a number of methods that can be used to collect saliva for cotinine analysis (Schramm *et al.*, 1992; Bernert *et al.*, 2000). Schneider and co-workers (1997) looked at salivary cotinine levels as a function of the collection method (Schneider *et al.*, 1997). Unstimulated salivary cotinine levels were compared with saliva collected by stimulation with a) sugar cubes and b) paraffin wax. In the sugar-stimulated saliva, cotinine levels were 26% below unstimulated levels, while wax-stimulated saliva yielded levels 6% below those of unstimulated saliva. The authors postulated that the reason for the difference may lie in the pH changes which alter with the salivary flow

rate. Cotinine has a pKa close to the pH of saliva and plasma. As the pH of unstimulated saliva is less than that of stimulated saliva, a basic compound such as cotinine would be influenced by the flow. Under more acidic conditions such as those produced by unstimulated saliva, there would be higher concentrations of cotinine available. Thus, as flow rate is increased with stimulation, less of the substance would be captured for measurement.

Although salivary cotinine is used in smoking cessation trials, often details of collection methods are not given, and it is not possible to determine whether the saliva collected is stimulated or unstimulated.

2.3 Use of Serum

Serum was probably the first medium to be used in cotinine analysis. The main disadvantage of serum is that it is invasive to collect, though it may be the sample of choice in most clinical settings, especially if patients are having blood taken for other reasons (Scott *et al.*, 2001). Serum samples have been used to determine smoking status in head and neck cancer patients (Hald *et al.*, 2003), follow-up care for patients with myocardial infarct and angina (Jolly *et al.*, 1999) and patients attending a bronchoscopy clinic (Lewis *et al.*, 2003).

Serum samples can be used to detect cotinine at low levels, such as that found through environmental exposure, though as previously stated, it can be invasive to collect.

2.4 Use of Urine

Urine is often the sample of choice in passive smoking studies, particularly if related to children (Blackburn *et al.*, 2003). Venepuncture is considered unsuitable and it may be difficult to obtain a salivary sample, especially in young children.

Urine sample collection is affected by diurnal rhythm, with lower excretions observed in the morning (de Weerd *et al.*, 2002). Urine measurements therefore have to be subject to creatinine/cotinine correction, expressed as a ratio (ng/mmol creatinine).

2.5 Patients' Acceptability of Sampling Methodology

With regards to the patients' perspective, no published work has previously investigated patient acceptability of the different sampling methods used to collect biological samples for cotinine analyses.

2.6 Method of Analysis of Cotinine

The initial methods developed for cotinine analysis included gas-chromatography (GC) and gas-liquid chromatography, and these have been discussed in Chapter 1.

In the last decade, a microplate enzyme immunoassay (EIA) kit has become available in the UK (Cozart, UK). The advantages of these kits are they do not require large, expensive equipment such as GC, and are relatively easy to handle. However, they are largely unevaluated in the UK.

2.7 Aims

The main aim, therefore, of this study was to measure and compare cotinine levels using the microplate enzyme immunoassay technique in a variety of biological fluids, collected from a group of patients, both smokers and non-smokers, recruited in an outpatient dental hospital department. Further aims were to:-

- a) Correlate self-reported smoking exposure data with the biochemical determination of cotinine levels, in the various body fluids, and to
- b) Compare levels of patient acceptability concerning the differing methods of sample collection.

2.8 Methods

2.8.1 Recruitment

Following approval from the Greater Glasgow Area Dental Ethics Committee (Appendix 2), recruitment was via patients attending the Oral Medicine outpatient clinic at Glasgow Dental Hospital and School. Copies of the patient information and consent forms are shown in Appendix 3. Initially, smokers were invited to participate, and non-smokers were then recruited, in an attempt to match age and gender to the first group. Data were collected over a 3-month period in early summer, by two student researchers and one academic researcher. A convenience sample was used, with as many patients recruited as possible within the available timeframe. The age range for the participants was 16 to 75 years.

Exclusion criteria included medical conditions such as an incipient diagnosis of oral carcinoma or medication affecting salivary function. For smokers, only those who used cigarettes were included in the study. Those individuals who smoked a pipe or used

cigars were excluded, as were any individuals currently using nicotine replacement therapy.

2.8.2 Self-reported Smoking Status

Participating patients were asked to fill in a questionnaire about their tobacco smoke exposure (see Appendix 4). The questionnaire sought information on daily number of cigarettes smoked, time of first cigarette of the day, inhalational habits and brand and tar levels of current cigarettes used. The time elapsed since the most recent smoking occasion was also noted. For non-smokers, information on exposure to tobacco smoke both at home and in the workplace was collected. Additionally, details relating to tobacco smoke exposure in the last 24 hours were recorded.

2.8.3 Sample Collection

Samples were then collected from each patient in the following order:

- 1) an unstimulated sample of saliva was collected by asking the patient to drool into a universal container (minimum volume of 3ml was collected).
- 2) a sample of stimulated saliva was collected by asking the patient to chew the cotton wool roll from a Salivette collection device (Sarstedt Aktiengesellschaft & Co, D-51588 Numbrecht, Germany). When saturated, this was removed from the mouth and placed into the salivette.
- 3) a sample of blood (5ml) was collected in a plain container using standard venepuncture techniques. This was collected by the student researchers and clinic nurse who was experienced in venepuncture.
- 4) a sample of urine (25ml) was collected in a plain universal container.

2.8.4 Patient Acceptability

Patients were then asked to fill in a short questionnaire concerning the acceptability of the four different methods of sample collection (see Appendix 4). A four-point Likert Scale was used which asked the respondents to rate the sample collection from 'completely unacceptable' to 'completely acceptable'.

2.8.5 Storage of Samples

Blood samples were stored in a fridge overnight, to allow clotting before the serum was separated and stored at -20°C . Stimulated saliva samples, collected using the Salivette devices, were centrifuged at 3000 rpm at 1200g for 10 min. The supernatant was then removed and stored at -20°C . The unstimulated saliva and urine samples were stored at -20°C . On the day of analysis, the unstimulated saliva was thawed and centrifuged and the supernatant transferred to inert plastic tubes.

2.8.6 Measurement of Cotinine

Cotinine concentrations were measured using a microplate enzyme immunoassay (Cozart Biosciences Ltd, Abingdon.UK).

Different versions of the assay, with appropriate standards, were used for each of the three biological matrices. Quality control material was prepared by spiking cotinine-free serum, urine and saliva with a cotinine standard (Sigma Chemicals) to give two levels, low and high within each standard range for each matrix. Where required, dilutions of the patients' samples were made using cotinine-free serum, urine and in the case of saliva, deionised water. Serum and salivary cotinine concentrations were expressed as ng/ml. Urine creatinine was measured by the kinetic Jaffe reaction on an

Olympus 640 analyser (Olympus UK Ltd, Southall, UK). To take account of urine dilution, all urine cotinine results were expressed as a ratio (ng/mmol creatinine).

A cut-off of 15ng/ml of cotinine was used to differentiate smokers from non-smokers in serum and saliva. For the urine sample analysis, a cut-off of 50ng/ml of cotinine was used to determine smokers.

2.8.7 Statistical Analysis

2.8.7.1 Comparisons of Cotinine Levels

When comparing smokers and non-smokers, it was necessary to logarithmically transform the data, due to greatly differing variances in the cotinine levels. Subsequent analysis was performed on the transformed data and reported confidence intervals to compare smokers and non-smokers are for the ratios of the geometric means. Similar analysis was required when comparing non-smokers who were exposed/not exposed to smoke.

For smokers and non-smokers separately, a repeated measures analysis of variance was used to determine whether there were any significant differences between the four collection methods in terms of mean cotinine levels. Subsequent follow-up multiple comparisons were carried out to identify which methods differed significantly. Generalised linear models were used to identify which self-reported factors, for smokers and non-smokers separately, had a significant effect on the cotinine levels, again with suitable follow-up multiple comparisons where necessary.

2.8.7.2 Analysis of Patient Acceptability Questionnaire

Simple column percentages of the responses of the trial participants with regards to 'very acceptable', 'moderately acceptable' 'tolerable' and 'not acceptable', with respect to each of the four collection methods were calculated.

2.9 Results

In total, 80 patients were recruited. Of the participants, 49 (25 male, 24 female) were smokers (61%) and 31 (15 male, 16 female) were non-smokers (39%). The mean age of the smokers was 44.0 years (SD 18.0 years) and for the non-smokers 46.5 years (SD 16.7 years). Thirty-eight (48%) of the participants were from relatively affluent backgrounds, i.e. residing in DEPCAT 1-4 areas (21 smokers and 17 non-smokers).

2.9.1 Comparison of Smokers v Non-Smokers

The mean cotinine level for the four fluids, for smokers and non-smokers separately, is shown in Table 2.1, together with the 95% confidence interval for the ratio of the geometric mean cotinine levels (smokers / non-smokers). Corresponding p-values from the 2 sample t-tests of mean levels of cotinine in smokers and non-smokers are also given.

Table 2.1 Mean Levels of Cotinine (ng/ml) for Smokers and Non-Smokers for each Sampling Method

	Smokers (n=49)	Non-Smokers (n=31)	95% CI**	
	Mean (stdev)	Mean (stdev)	(S / NS)	p-value
Serum	328.4 (207.5)	3.6 (2.8)	(59.7, 111.7)	<0.001
Stimulated Saliva	194.3 (122.5)	2.0 (0.9)	(28.5, 105.4)	<0.001
Unstimulated Saliva	314.0 (171.9)	1.6 (1.2)	(120.8, 235.5)	<0.001
Urine*	302.5 (244.0)	1.1 (1.9)	(224.9, 776.3)	<0.001

*Units are ng/mmol

**CI is for ratio of geometric mean of Smokers to geometric mean of Non-Smokers

A clear differentiation between the smokers and non-smokers was seen (with $p < 0.001$ for all fluids) with confidence intervals illustrating the much greater mean cotinine levels of smokers. The mean level of cotinine in non-smokers in all the fluids was below 10ng/ml, whereas the mean level of cotinine in the smokers varied from 194ng/ml in stimulated saliva to 328ng/ml in serum.

2.9.2 Comparison of Collection Methods

Repeated measures ANOVA indicated that there were significant differences in the mean cotinine levels between the four collection methods, for both smokers and non-smokers (both $p < 0.001$). Subsequent multiple comparisons indicated that, for smokers, the cotinine levels in serum, urine and unstimulated saliva were significantly greater on average than the levels found in stimulated saliva (Table 2.2). For non-smokers, where cotinine was being measured in very small amounts, there were significant differences between the serum and all other types of sample, with the mean serum level being significantly higher. When comparing the urine and stimulated saliva in non-smokers,

the mean level in the stimulated saliva was significantly higher. This last finding is the opposite relationship to that found with these two samples in smokers, where the mean level of cotinine in urine is higher than that found in the stimulated saliva.

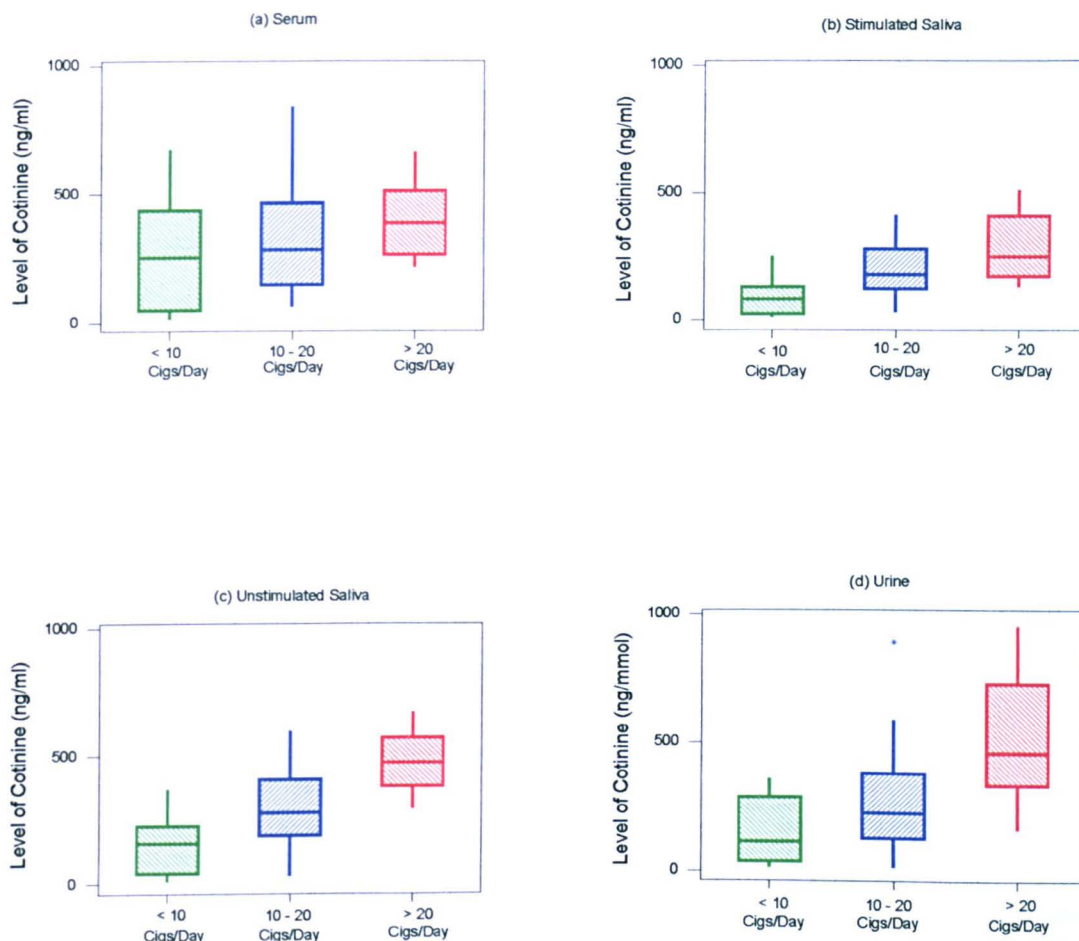
Table 2.2 Multiple Comparisons of Sampling Methods for Smokers and Non-Smokers

		95% Simultaneous CI for Difference in Average Cotinine Levels	
Fluid	- Fluid	Smokers (n=49)	Non-Smokers (n=31)
Serum	- Stim. Saliva	(59.7, 217.7)	(0.9, 2.5)
Serum	- Unstim. Saliva	(-63.7, 93.2)	(1.2, 2.8)
Serum	- Urine	(-52.0, 103.9)	(1.8, 3.4)
Urine	- Stim. Saliva	(33.7, 191.8)	(-1.7, -0.1)
Urine	- Unstim. Saliva	(-89.7, 67.3)	(-1.3, 0.3)
Unstim. Saliva	- Stim. Saliva	(44.4, 203.5)	(-1.2, 0.4)

2.9.3 Relationships between Self-Reported Data and Cotinine levels for Smokers

Results from generalised linear models, incorporating number of cigarettes smoked per day (<10, 10-20 or >20), tar level of cigarettes smoked (low, medium or high) and inhalational habits (slightly, moderately or deeply) for each of the collection methods separately, suggested that the only factor having a significant influence on the smokers' cotinine levels was number of cigarettes smoked per day (NOCS). The boxplots shown in Figure 2.1 show a cotinine dose-response relationship with NOCS. This dose-response relationship between cotinine level and NOCS was statistically significant for stimulated saliva, unstimulated saliva and urine (all $p < 0.001$) but was not statistically significant for serum ($p = 0.291$).

Figure 2.1 Cotinine Dose-response for Smokers Categorised as Low, Medium and Heavy, in Stimulated & Unstimulated Salivas, Serum and Urine



For stimulated saliva, the mean cotinine level for <10 cigarettes/day was significantly lower than that for 10-20 cigarettes/day and >20 cigarettes/day, but there was no significant difference between the mean cotinine level for 10-20 and that for >20 cigarettes/day. For unstimulated saliva, there was a significant difference between each of the three categories of NOCS. For urine, there was no significant difference between the average levels of cotinine for <10 and 10-20 cigarettes/day, but both of these had on average lower levels of cotinine than the >20 cigarettes/day category.

2.9.4 Relationships between Self-Reported Data and Cotinine levels for Non-Smokers

For non-smokers, generalised linear models were used to determine which of the three factors – exposed to passive smoke at home (yes or no), at work (yes or no) and exposed to passive smoke in the previous 24 hours (yes or no) – had a significant influence on the mean cotinine level, for each of the four collection methods in turn. For each of the fluids, the most dominant factor was exposure to smoke at home. This factor had a significant effect on the average cotinine levels of stimulated saliva, unstimulated saliva and urine (all $p < 0.05$). For each of these fluids, exposure to smoke at home significantly increased on average the mean level of cotinine, compared to the mean level of cotinine of participants not exposed to smoke at home (see Table 2.3).

Table 2.3 Mean Levels of Cotinine (ng/ml) for Non-Smokers for each Sampling Method by Exposure to Smoke at Home

	Exposed to Smoke at Home (n=10) Mean (stdev)	Not Exposed to Smoke at Home (n=21) Mean (stdev)	95% CI** (Exposed / Not Exposed)	p-value
Serum	5.4 (4.7)	2.9 (0.8)	(0.4, 1.4)	0.25
Stim. Saliva	2.7 (1.4)	1.7 (0.4)	(0.5, 0.9)	0.02
Unstim. Saliva	2.5 (1.9)	1.3 (0.4)	(0.4, 1.0)	0.04
Urine*	2.3 (2.0)	0.6 (1.5)	(0.1, 0.5)	<0.01

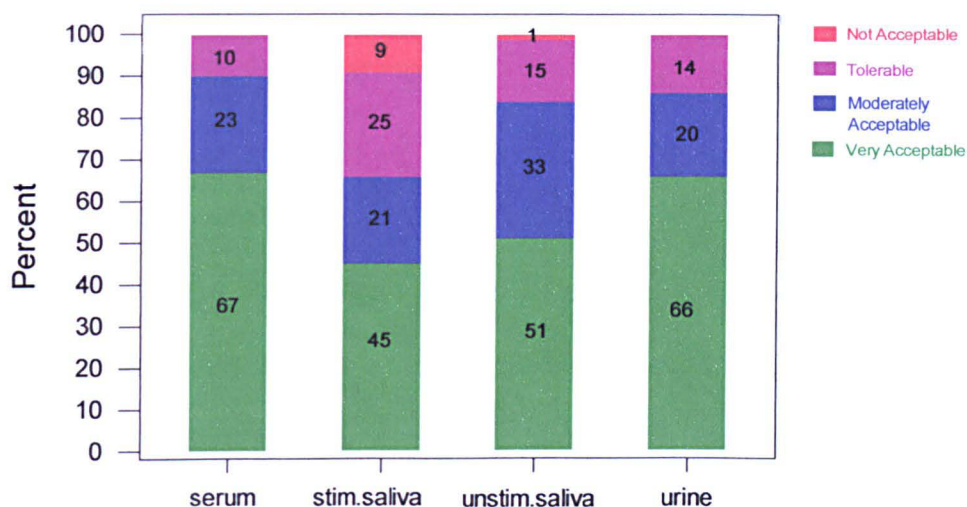
*Units are ng/mmol

**CI is for ratio of geometric mean of Exposed to geometric mean of Not Exposed

2.9.5 Patient Acceptability of Each Collection Method

Figure 2.2 gives the percentages of patients who found each of the four collection methods ‘very acceptable’, ‘moderately acceptable’, ‘tolerable’ and ‘not at all acceptable’.

Figure 2.2 Patient Acceptability of Collection Methods



There was no difference between the patterns of acceptability of smokers and non-smokers. High numbers of patients found both serum and urine collection methodologies ‘very acceptable’ (67% and 66% respectively), significantly greater than that for the stimulated saliva collection (45%). No participant rated the serum or urine collection methods as being ‘not at all acceptable’, whilst almost 1 in 10 (9%) found collection of the stimulated saliva ‘not at all acceptable’. The unstimulated saliva fared better than the stimulated saliva, with 51% of the participants rating the former collection method as ‘very acceptable’ and only 1% ‘not at all acceptable’.

2.10 Discussion

2.10.1 Recruitment

In total, 80 patients were recruited, 49 smokers and 31 non-smokers. It is acknowledged that the utilisation of a convenience sample may have resulted in recruited participants not necessarily being representative of the typical oral medicine patient population. Although a reasonable number of participants were recruited, the matching of non-smokers and smokers was incomplete due to time constraints, resulting in an unequal number of patients in the two groups.

2.10.2 Sample Collection

For monitoring purposes within a smoking cessation trial, usually only one type of biological sample would be collected. This study was more unusual in that a variety of samples were collected which allowed examination of the inter-relationships between the different fluids. This study was also cross-sectional and was not being used to verify quit attempts.

2.10.3 Differentiation between Smokers and Non-Smokers

Using the appropriate microplate enzyme immunoassay kit for each type of sample, there was clear differentiation between smokers and non-smokers in this study. This agrees with the findings of previous studies (Velicer *et al.*, 1992).

2.10.4 Comparison of Cotinine in Different Samples

With regard to the relationship between the two methods of salivary collection, the mean level of cotinine in smokers was found to be greater in the unstimulated (314ng/ml) compared to the stimulated (194ng/ml) saliva. These findings were

consistent with those of Schneider *et al.* (1997) who postulated that the reason for the difference may lie in the pH changes which alter with salivary flow rate.

A number of papers have compared cotinine levels in different biological samples. The half-life of cotinine in saliva and serum is approximately the same, and cotinine concentrations in these two matrices have previously been found to be correlated. Bernert and co-workers (2000) looked at the relationship between serum and saliva (collected via salivette devices) and found a simple linear relationship of serum cotinine levels being 10% above or below the given salivary levels.

However, in the present study, serum levels were found to be more closely correlated with unstimulated than stimulated saliva. For smokers, the serum cotinine was on average 4% and 41% greater than the unstimulated and stimulated saliva respectively.

McAdams and Cordeiro (1993) looked at determining the level of cotinine in serum, urine and oral samples. Salivary samples in this study were collected using the OrasSure system (North *et al.*, 1993). This collection device consists of an absorbent paddle, which is placed in the patient's mouth, and once the pad is saturated it is inserted into the collection tube ready for storage, prior to analysis.

The authors stated that the results of the assignments in all three matrices matched the self-reported smoking status perfectly. However, this was a small study with only 20 participants, both smokers and non-smokers, and the focus of the paper was on the development of a gas-chromatography method of analysis. No attempt was made to look at the relationship between the cotinine in the three samples.

An older study compared serum, saliva and urine in non-smokers, passive and active smokers (Wall *et al.*, 1988). This study had a sample of 98 subjects. More unusually, these individuals were asked to collect samples of their saliva and urine in their own homes. Such samples are usually collected for quality assurance purposes under the supervision of the researchers, who, in this study, took blood for serum cotinine estimation. Serum and saliva cotinine results could not discriminate between non-smokers and passive smokers. Mean urine cotinine was higher in passive smokers than non-smokers but there was a great deal of subject overlap. Cotinine in all body fluids could separate active smokers from the other groups. Additionally, among smokers, light smokers had lower levels than heavier smokers.

2.10.5 Cotinine Dose-Response

A cotinine dose-response relationship to nicotine exposure is important as it helps to quantify the relative risk that patients are undergoing. In this study, the two salivary samples and urine samples were able to differentiate between categories of light, medium and heavy smoker, whereas serum samples were not able to exhibit this finding. Machacek and Jiang (1986) found similar results, with little association between cotinine concentrations in plasma and number of cigarettes smoked. With regards to saliva and cotinine levels, Etter *et al.* (2000) found cotinine concentration to be moderately associated with the number of cigarettes per day.

In longitudinal studies of smoking cessation or reduction in smoking, the ability to differentiate between the categories of smoking may be of use in looking at reduction in nicotine exposure. It could be used to differentiate between those smokers who say they have reduced, but continue to compensatory smoke by inhaling more deeply or by

smoking more of their cigarettes, compared to those who cut down their smoking prior to quitting totally.

As discussed previously, this work was cross-sectional in nature, and exhibited a dose-response on a population basis. With regards to smoking cessation or reported reduction, a further longitudinal study is required to see whether the cotinine levels at baseline for a cohort of patients correlates with patients' self-reported smoking exposure at further time points such as 3 and 6 months.

2.10.6 Patient Acceptability

Patient acceptability of the different methods of sample production provided some unexpected findings. It was postulated that patients might rate venepuncture least favourably because of the invasive nature of the technique, when surprisingly they rated the stimulated saliva collection most negatively. Some participants found the chewing of the cotton wool roll an unpleasant sensation and, in extreme cases, felt nauseous, which may have led to a poor acceptability rating being recorded. Using a cotton wool roll to collect saliva in this way is not the most common method, though previous published work has used this methodology (Roy *et al.*, 1996; Croucher *et al.*, 2002). A more usual method to stimulate saliva would be the use of paraffin wax to induce salivary flow (Kivela *et al.*, 2003). From a participant's point of view, the unstimulated saliva appeared to be the more acceptable of the two salivary collection methods, and hence would be the choice for any future work. However, acceptability levels associated with alternative means of stimulating saliva would require further investigation.

The high acceptability of the blood sampling methodology may be related to the setting in which this cross-sectional study took place: a dental hospital oral medicine department where venepuncture is often a routine part of investigation. It was decided to carry out this work in an oral medicine setting because it was felt that it was more ethical to recruit patients who were undergoing this procedure anyway as part of their treatment planning. It is postulated that work carried out in a different dental setting such as general dental practice or a periodontal clinic may yield differing results in terms of patient acceptability of collection methods.

The operator effect has yet to be investigated. Samples were collected by the student researchers who had undergone special training in venepuncture and with increasing practice would have become more proficient at the technique. The nurse who routinely carried out this procedure could be expected to be skilled in this area. It is postulated that in a different setting such as general practice, dental practitioners who are not routinely used to taking blood samples may not want or feel they have the skills to use this technique.

2.10.7 Suitability of Kits

One aim of this study was undertaken to determine whether EIA kits could be used to determine the smoking status of patients, recruited to a future smoking cessation trial within a dental hospital setting. The immunoassay kits provided an acceptable means of analysing cotinine in this current sample of patients. The advantages of these kits included availability (currently there is no access to GC facilities for cotinine analysis in Scotland) and economic considerations. These kits were sufficiently sensitive to distinguish between categories of smoker and non-smoker.

2.11 Conclusions

For future smoking cessation work, baseline verification of cotinine levels, followed by cotinine assessment once smoking cessation interventions have taken place offer a good means of monitoring and evaluating the process of smoking cessation interventions as they are delivered.

All matrices, including serum, urine and the two methods of collecting saliva, were successful in differentiating between smokers and non-smokers.

The use of EIA kits proved to be a suitable alternative to GC analysis on the basis of performance, cost, accessibility and the sample size involved in this study.

With regards to choice of sample for oral health staff, salivary samples, whether stimulated or unstimulated would appear to be the most appropriate for use within a dental setting. Levels of cotinine obtained with unstimulated saliva were higher, and sample collection was more acceptable to the patient. Stimulated saliva yielded lower levels of cotinine and was less acceptable to the patients. If stimulated saliva sample collection was required, it may be necessary to look at other methods of stimulating saliva, such as the use of paraffin wax.

Chapter 3

Smoking-Related Behaviour Change in Periodontal Patients given ‘Brief’ Smoking Cessation Advice and Nicotine Replacement Therapy, Delivered by Dental Hygienists: A Randomised Controlled Trial

3.1 Introduction

Tobacco use is the single biggest contributor to ill health, and is the most important preventable cause of death in the UK (Callum, 1998). As outlined in Chapter 1, in addition to being implicated in coronary heart disease, lung and other cancers, smoking also has a profound effect on the oral tissues. Cigarette smoking is associated with increased prevalence and severity of periodontitis and smokers suffer from more tooth loss (Krall *et al.*, 1997; Tonetti, 1998). In addition, the risk of oral cancer and potentially malignant lesions is higher amongst smokers compared to those who have never smoked. Patients who smoke have a six-fold increased risk of developing oral leukoplakia compared with non-smokers (Baric *et al.*, 1982).

There is growing awareness and interest in the role that dental health professionals can play in helping their patients quit the tobacco habit, whether in secondary or primary care (Chestnutt & Binnie, 1995; Macgregor, 1996; McCann *et al.*, 2000; Watt & Daly, 2003; John *et al.*, 2003). Most research has focussed on dentists and their contribution, but increasingly interest is being shown in the role that dental hygienists can play (Chestnutt & Binnie, 1996; Dykes *et al.*, 2001; Helgason *et al.*, 2003).

One trial in the UK has shown that the dental team can be involved in delivering smoking cessation advice, with a resultant quit rate of 11% at nine months (Smith *et al.*, 1998). However, this trial was not of a randomised controlled trial design.

One US study utilised dental hygienists to give advice on quitting to two groups of patients, the first of whom smoked cigarettes, while the second used smokeless tobacco. It was found that the intervention was effective for smokeless tobacco, but not for cigarettes (Severson *et al.*, 1998). However, an earlier study utilising dental hygienists to give advice to patients who smoked cigarettes, found a cessation rate at six months of 14.6% (Secker-Walker *et al.*, 1988). Neither of these studies used any form of biochemical validation and relied on self-report only, nor did the latter study have a control group.

Therefore, within the UK, there is the need to investigate more fully the potential effectiveness of dental hygienists in delivering smoking cessation advice, by running a trial with an RCT design, and with the primary outcome of smoking cessation, biochemically validated.

3.2 Aim

The aim of this trial was to examine the feasibility and efficacy of a smoking cessation intervention, delivered by dental hygienists, in a cohort of periodontal patients attending an outpatient dental hospital department.

The research question was:

What is the efficacy of a smoking cessation programme, based on the 'brief intervention' and delivered by dental hygienists?

- Success being measured both in terms of primary (absolute cessation) and secondary (reduction in smoking behaviours/change in psychological readiness for behaviour change) outcomes.

3.3 Material and Method

3.3.1 Trial Design

A randomised controlled trial design was considered the most appropriate methodology.

The setting for the intervention was the Periodontology Department of Glasgow Dental Hospital and School. With respect to the delivery of the intervention, the three staff dental hygienists, working within the Periodontology Department, participated in the trial and gave the patients smoking cessation advice. For the purposes of confidentiality, the hygienists were colour-coded Red, Green and Blue, with respect to the project administration and analysis. In addition, a research dental hygienist helped with patient follow-ups.

3.3.2 Training of Dental Hygienists

Prior to undertaking the delivery of smoking cessation advice, the hygienists attended training sessions in smoking cessation. Topics covered included basic smoking cessation training (2 sessions), nicotine replacement therapy training (1 session) and smoking cessation trial methodology (1 session). Further information on the course content and personnel involved in delivering the training is to be found in Appendix 5.

3.3.3 Ethical Approval

Ethical approval was sought from the local Area Dental Ethics Committee, and approval was gained in February 2001. A copy of the Letter of Approval is attached in Appendix 6.

3.3.4 Patient Recruitment

Clinical activity figures indicated that, between April 1999 and March 2000, there were 1554 newly referred patients examined by consultants within the Department of Periodontology at Glasgow Dental Hospital and School. Of this pool of patients, approximately 50% are referred to the staff dental hygienists for treatment. An audit carried out within the Department in the summer of 2000 found that around 37% of new patient referrals were smokers. Based on this information, it was estimated that there would be a pool of approximately 275 new patients annually, who smoked, and who were referred to the staff hygienists for treatment.

Prior to the start of the smoking cessation study, as part of normal professional practice, all new patients who smoked, on attending the Consultant Periodontal Clinics, received information on the role that tobacco plays in periodontal disease and ‘very brief’ advice to quit by one of the four consultants assessing their periodontal health.

From the cohort of new patients who attended from April 2001, and who were to be referred to the dental hygienists for treatment, those who smoked more than ten cigarettes a day were offered the opportunity to participate in the smoking cessation trial. Exclusion criteria included patients aged below 18 years, those already in receipt of NRT or currently undergoing smoking cessation therapy, or patients with complex

medical histories. Recruitment was via the patient's consultant who explained the nature of the trial, and gave the patient the study information sheet and asked them to sign the consent forms. It was made explicit that the patient would not necessarily be allocated to receive further advice and help in smoking cessation. Copies of the patient consent and information forms are in Appendix 7.

3.3.5 Sample Size Calculation

The sample size calculation was based on the secondary outcome of reduction in cigarette consumption. Macgregor (1996) reported that just over 25% of subjects in the control group had some reduction in cigarette consumption.

For this calculation, success was defined as being a reduction in smoking activity. It was deemed of interest to consider a projected success rate of 25% in the control group with a minimum projected success rate of 50% in the intervention group. The sample size calculation was therefore based on being able to detect such a minimum difference, using a chi-squared test with 80% power and a two-tailed significance level of 5%. This calculation resulted in the requirement of at least 60 individuals within each group to be followed-up at 3 months.

3.3.6 Baseline Questionnaire Data Collection

To obtain baseline information from the smokers, a questionnaire containing both open and closed questions was designed. Demographic information including name and address, hospital number, age, gender, occupation and information on postal code (to enable DEPCAT analysis) was requested from the participants.

3.3.6.1 Assessment of Nicotine Dependence

A further section in the questionnaire assessed the patient's level of nicotine dependence, using standard scales (*Heaviness of Smoking Index/Fagerstrom Test for Nicotine Dependence/Fagerstrom Tolerance*).

The *Heaviness of Smoking Index* is comprised of two questions which determine the number of cigarettes smoked per day, and the timeframe between waking in the morning and having the first cigarette of the day (Heatherton *et al.*, 1991).

The *Fagerstrom Test for Nicotine Dependence (FTND)* includes the above two questions and four additional questions covering the cigarette of the day the respondent would most hate to give up, whether smoking was more frequent during the first hours of the day, whether smoking took place when ill and whether there was difficulty refraining from smoking in public places (Heatherton *et al.*, 1991).

The *Fagerstrom Tolerance Score* includes all of the six questions detailed above and two further questions concerning the habit of inhalation of smoke, and the nicotine level of the cigarettes (Fagerstrom, 1978).

3.3.6.2 Assessment of Motivation to Stop Smoking

Readiness to quit is often measured using a version of 'Stage of Change', though the questions used are not so easily obtained via the literature, nor are they as standardised, as the FTND. Therefore, following a search of the literature, an adapted instrument containing elements of '*Stage of Change*' (after Prochaska & DiClemente, 1983), was designed using the terms 'contented smoker', 'concerned smoker' and 'wanting to quit'

A 'contented smoker' is defined as someone who does not wish to stop smoking (a 'precontemplator'), a 'concerned smoker' is defined as someone who wishes to stop smoking sometime in the next six months (but not in the next month) (a 'contemplator'), and those in the category 'want to quit' would wish to do so at sometime in the next month (i.e. are in the 'preparation' phase).

Motivation to quit was also assessed using two standard scales measuring strength of motivation and desire to quit (Foulds, 1996). These were measured on a five-point Likert scale, ranging from very positive to very negative, encompassed by the terms 'Yes, definitely' to 'Definitely not'. Questions on this scale were: 'Would you give up smoking altogether if you could do so, easily?' and 'How much do you want to stop altogether?'

3.3.6.3 Reasons for Stopping Smoking and Quitting History

Included in the questionnaire was a section on reasons for wanting to stop smoking. Options provided included health, expense, 'not fair on other people' and 'don't like being addicted'. Patients were also asked what they perceived to be their biggest problem in quitting. Recent quitting history was also elicited via questions on quit attempts in the last year, including specific questions on whether they had had two or more quit attempts or a quit attempt lasting longer than one week. Other environmental exposure to tobacco was determined by asking the respondents whether anyone at work or at home smoked.

The questionnaire was piloted with 15 smokers who attended the staff hygienists after which very minor modifications were made with regard to layout. The final questionnaire used in the study is to be found in Appendix 8.

3.3.7 Baseline Biochemical Assessment of Exposure to Nicotine using Cotinine (COT) and Carbon Monoxide (CO)

3.3.7.1 Cotinine

To assess the patient's current exposure to nicotine, a baseline salivary sample of unstimulated saliva was collected for cotinine (COT) analysis. Samples were stored at -20°C , prior to being analysed by Mr Bill Borland, a specialist toxicologist biochemist at Gartnavel General Hospital in Glasgow. EIA (enzyme immunoassay) kits were used to determine the level of cotinine in the samples (Cozart UK). The detailed methodology with regard to the cotinine analysis is outlined in Chapter 2.

3.3.7.2 Carbon Monoxide

In addition to the sample of saliva taken for cotinine analysis, an exhaled air sample was collected via a carbon monoxide (CO) monitor. The monitors used were picoSmokelysers (Bedfont Scientific). The patient blew into the monitor using a disposable mouthpiece connected to a T-piece, which in turn was linked to the monitor and screen. A reading of CO, in ppm, was shown within seconds on the LED display. These monitors were provided on long-term loan by *Smoking Concerns* (Health Promotion, Greater Glasgow NHS Board). The monitors were calibrated regularly in accordance with the instructions supplied by the manufacturers.

3.3.8 Randomisation Process

A two stage randomisation process was used, firstly to allocate randomly recruited patients to a staff hygienist, and then to allocate randomly the patient to a group (intervention or control).

3.3.8.1 Randomisation of Patient to Hygienist

The three staff hygienists were each allocated a colour (Red, Blue and Green) for identification purposes.

Prior to the commencement of patient recruitment, a randomisation list was produced by the project statistician, using the random permuted blocks method, to ensure exactly equal numbers of patients were allocated to each hygienist after every 18 patients recruited. The randomisation list was then transcribed into a log book, which contained sequential patient log numbers and against each log number, the allocated hygienist. When a patient was recruited into the study, the patient was assigned the next available patient log number, from which the allocated hygienist was deduced.

3.3.8.2 Randomisation of Patient to Group

Recruited patients, having been randomly allocated to a hygienist, completed the baseline questionnaire at the first visit, from which information was extracted for use in randomising the patient to a group.

The information used in the randomisation process was: -

- **Age** (<34 , 35-44, 45-54, >55 years)
- **Sex** (Female, Male)
- **DEPCAT** (1 - 2; 3 - 5; 6 - 7).
- **Level of Nicotine Dependence** (6 and below, above 6)
- **'Stage of Change'**
 - (Stage 1 – 'contented smoker')
 - ('precontemplator')
 - (Stage 2 - 'concerned smoker')
 - ('contemplator')
 - (Stage 3 – 'want to stop')
 - ('preparation')

Patients were randomly allocated to either the intervention or control group using the minimisation method (Pocock, 1983), which is a form of stratified randomisation. The aim of this was to achieve balance in the numbers of participants in the two groups with regard to the above five factors.

The minimisation method cannot be used to prepare a randomisation list in advance. Instead, a continually up-to-date record of group allocations by the five patient factors was kept, using sets of index cards (one set per hygienist), with one index card for each level of each of the five factors. To assign a newly recruited patient to a group, the information from the baseline questionnaire was collated and the five relevant index cards were pulled out and the number of patients in each group, for this combination of patient factors, calculated.

Rather than strictly allocating the new patient to the group with the smallest number of patients to date, a random element was introduced, whereby a previously prepared randomisation list was used to allocate the patient to the group with fewest patients to date, with a given probability less than one. When, for the given combination of the five patient factors, there were equal numbers of patients in the two groups to date, a pre-prepared simple randomisation list was used to allocate the patient to a group.

Following randomisation, the hygienist was informed of the outcome and subsequently passed on the information to the patient at the following visit. The control group was given no further smoking cessation advice.

The intervention group within this study were given more advice and help as detailed below.

3.3.9 Protocol for Intervention Group

3.3.9.1 Structured Approach to Giving Smoking Cessation Advice -‘5As’

Patients were given advice on smoking cessation in a format based on the **5As** - *Ask* your patient, *Advise* your patient, *Assess* your patient, *Assist* you patient, *Arrange* follow-up for you patient (Table 3.1). These **5As** were to be reinforced at every visit.

In order to standardise the smoking cessation advice delivered by the three staff hygienists, a protocol checklist based on the **5As**, was customised for use in the study. This version is attached in Appendix 9.

Table 3.1 The 5As Protocol

Stage	Action
<i>Ask your Patient</i>	Ask about current smoking habits: (make comment about baseline information) <ul style="list-style-type: none"> • number of cigarettes, time to first cigarette • smoking pattern • smoking history • number of years as a smoker • quitting history
<i>Advise Your Patient</i>	Advise quitting tobacco use <ul style="list-style-type: none"> • advice is to be clear, personalised and firm • emphasise not only the links with periodontal disease and oral cancer, but also to the general health risks
<i>Assess your Patient</i>	Assess willingness to quit <ul style="list-style-type: none"> • What are the important reasons for them to give up, is it fitness, smoking near children etc? • Where are they on the 'Stage of Change' and when are they thinking of giving up? • a contented smoker – 'not at the moment' • a concerned smoker – 'within the next 6 months' • preparing to stop - 'within the next 30 days'
<i>Assist your Patient</i>	Assist patients who agree to stop <ul style="list-style-type: none"> • set a timescale for action • give information on the process of quitting, such as smoking cessation materials from <i>Smoking Concerns</i>, and <i>Aspire</i> (ASH/HEBS 2002) • review what helped and hindered from previous attempts • identify likely problems and appropriate strategies to overcome them, e.g. smoking and drinking etc, what to do about other smokers etc • enlist support of family and friends • plan how to cope with increase in food and drink • give advice, information and an offer of Nicotine Replacement Therapy (see below)
<i>Arrange follow-up</i>	Arrange follow-up appointments <ul style="list-style-type: none"> • reinforcement of 5As as part of periodontology (oral hygiene phase and treatment) visits • monitoring of patients progress, use of CO monitors at each visit

On the first visit after the patient had been randomised to the intervention group, the hygienist delivered the advice as per the above protocol. The approximate time taken for the delivery of the advice was 15 min. For subsequent appointments, hygienists filled in another '5As' checklist, personalising and developing an individual approach with each patient.

3.3.9.2 Nicotine Replacement Therapy (NRT)

The use of Nicotine Replacement Therapy (NRT) as part of treatment, is known to increase cessation rates and is an important adjunct to the provision of 'brief advice'. It is a well-accepted means of dealing with nicotine withdrawal.

The NRT used in the trial was the brand Nicorette (Pharmacia and Upjohn), and funding for this was provided by *Smoking Concerns*, Glasgow's Tobacco Control Project (Health Promotion Department, NHS Greater Glasgow). Patients in the intervention group who wished access to this form of support, were therefore offered NRT at no charge.

Only two forms of NRT were offered; patches and gum. It was decided that to offer additional types of NRT such as inhalers or tablets would be overly complicated, and as fairly small numbers of patients were involved, would pose stock control difficulties.

Nicorette patches are 16-hour patches and are designed to be used during waking hours and removed at night. Patches were available in 15, 10 and 5 mg doses of nicotine, and applied to the skin of the upper arm or thigh. Patients started at the high dosage patch, and stepped down to the medium dosage when they felt ready. Patches are not suitable

for those individuals who have widespread dermatological conditions, or an allergy to the adhesive.

Nicorette gum is available in 2 and 4 mg strengths. If a patient smoked more than 20 cigarettes per day, the 4 mg gum was recommended. The typical dosage is 10-15 pieces of gum per day. Gum is not suitable for patients with dentures. Patients were taught the correct technique for taking gum to ensure buccal absorption.

For audit purposes, dental hygienists filled in an internal (Glasgow Dental Hospital) prescription pad which recorded patient details and the amount and type of NRT prescribed. The NRT prescribing was underwritten by a dental surgeon (Mrs V. Binnie).

3.3.9.3 Patients who were Not Willing to Commit to Quitting

For some patients who did not feel able or ready to quit at the time of the initial intervention, various options were available as described in Table 3.2 below. For those patients who wanted to make some changes, the approach used is listed in the upper part of the table. For 'contented smokers', the delivery of the **5Rs** is recommended, as detailed in the lower half of Table 3.2.

Table 3.2 Protocol for Patients not Willing to Commit to Quitting

<i>Patients who agree to some change in smoking behaviour</i>	<ul style="list-style-type: none">• explain that smoking is a cyclical process and some behaviour change such as reducing number of cigarettes, making at least one quit attempt is partial success• look at reducing consumption of cigarettes• encouraged to make at least one quit attempt of 24 hours or longer
<i>Patients who DO NOT want to quit (5Rs)</i>	<ul style="list-style-type: none">• emphasise the relevant benefits for the patient• emphasise the risks of continuing to smoke• list the rewards from stopping• discuss the roadblocks to quitting (withdrawal symptoms, lack of support etc)• emphasise that repeat attempts are more successful

3.3.10 Protocol for Control Group

This group was given no further structured advice regarding smoking. However, if the patient raised the topic, this was dealt with using normal professional practice. Details of any such advice were recorded within the patients' notes.

3.3.11 Questionnaire Follow-up for Intervention and Control Groups at 3 and 6 Months

Patients were followed-up at 3 and 6 months after recruitment in the Periodontology Department. This included a questionnaire-based assessment of smoking behaviour.

The follow-up questionnaire asked about smoking behaviour during the previous three months, and patients were asked whether they considered themselves to be smokers or non-smokers. If they considered themselves to be quitters, they were asked about a quit

date, and whether they used pharmaceutical support in the form of NRT or Zyban. Patients who still considered themselves to be smokers were asked about any changes in smoking behaviour, including the number and length of any quit attempts in the previous three months, any reduction in smoking either by smoking less or inhaling less, or whether they had changed cigarette brands. Some of the questions had previously been used in a smoking cessation study in general practice (Butler *et al.*, 1999), whilst others were designed for this study (smoking less of a cigarette; inhaling less). Information was also collected on the participants current '*Stage of Change*'. Full copies of these questions are in Appendix 10.

3.3.12 Measures of Abstinence used to Determine Quitting

In this trial, the measure of point prevalence was used, with prolonged abstinence measures also reported for 6-month outcomes. Smokers were not asked if they 'had smoked, not even a puff, in the last fortnight', but as cotinine sampling was used, contact with nicotine could be established and verified over the previous week. This 7-day window is the suggested time frame for verifying smoking as suggested by Hughes *et al.* (2003). In the context of this study, participants were categorised as being prolonged abstainers if they were classified as definitive quitters at both 3 and 6 months.

3.3.13 Biochemical Follow-up of Intervention and Control Groups at 3 and 6 Months

As at baseline, a salivary sample was collected for cotinine (COT) analysis, and an exhaled air sample used for carbon monoxide (CO) analysis. Three and six-month saliva samples were collected in similar bottles to those used at baseline, but were labelled and colour-coded (red for 3 months and blue for 6 months) to aid identification during storage and analysis.

With respect to cotinine, a cut-off level of 20ng/ml was used in this study with a value below 20ng/ml generally indicating a non-smoker. With respect to the CO cut-off level used to determine smoker from non-smoker, a value of 9ppm or above indicated a smoker.

However, if there was evidence that a patient had been using NRT, a higher COT could be expected, and thus the smoker's classification of cessation was verified by the CO value. Furthermore, if a self-reported quitter, in the absence of self-reported NRT use, had a cotinine level higher than the cut-off stated, but the CO indicated that the individual was a non-smoker, cognisance was taken of the baseline measurements of COT to determine how much the nicotine loading had reduced.

3.3.14 Follow-up for Intervention and Control Groups at One Year

Attempts were made to contact patients at one year after recruitment, initially by telephone, and for those for whom it proved impossible to establish contact this way, follow-up via a postal questionnaire was attempted. Patients were asked whether they had quit or not, and if so, the date on which they quit. The self-reported quitters were also asked to provide a sample of saliva, to be posted to the dental school for cotinine

analysis. If the patient described themselves as a smoker, they were asked about the number of cigarettes they smoked, and the reasons for currently smoking. A copy of both telephone and postal questionnaires are to be found in Appendix 11.

3.3.15 Statistical Analysis and Data Handling

Information from the questionnaires and biochemical information regarding CO and COT levels was scribed onto a data entry form designed in Microsoft Access. Using these forms, data were then manually entered into separate Microsoft Access databases for the following time points in the trial (baseline, 3 and 6 months), and an Excel database for the 12 month results. Data were then exported for statistical analysis into Minitab (version 14) and StatXact (version 4).

Statistical analyses consisted predominately of comparing the intervention and control groups in terms of baseline information (both questionnaire and biochemical data) and also the primary outcomes at 3, 6 and 12 months and secondary outcomes at 3 and 6 months after recruitment.

When comparing the two groups, continuous, normally-distributed data were summarised by means and standard deviations and analysed using two-sample t-tests and confidence intervals. Data which were numerical but not normally-distributed were summarised by medians and inter-quartile ranges and groups compared using Mann-Whitney tests and confidence intervals. When comparing groups in terms of categorical variables, tables were produced to summarise the data, which were analysed using chi-squared tests. The primary and secondary outcomes, which were binary variables, were

compared between groups using tests of equal proportions and confidence intervals for the difference between groups.

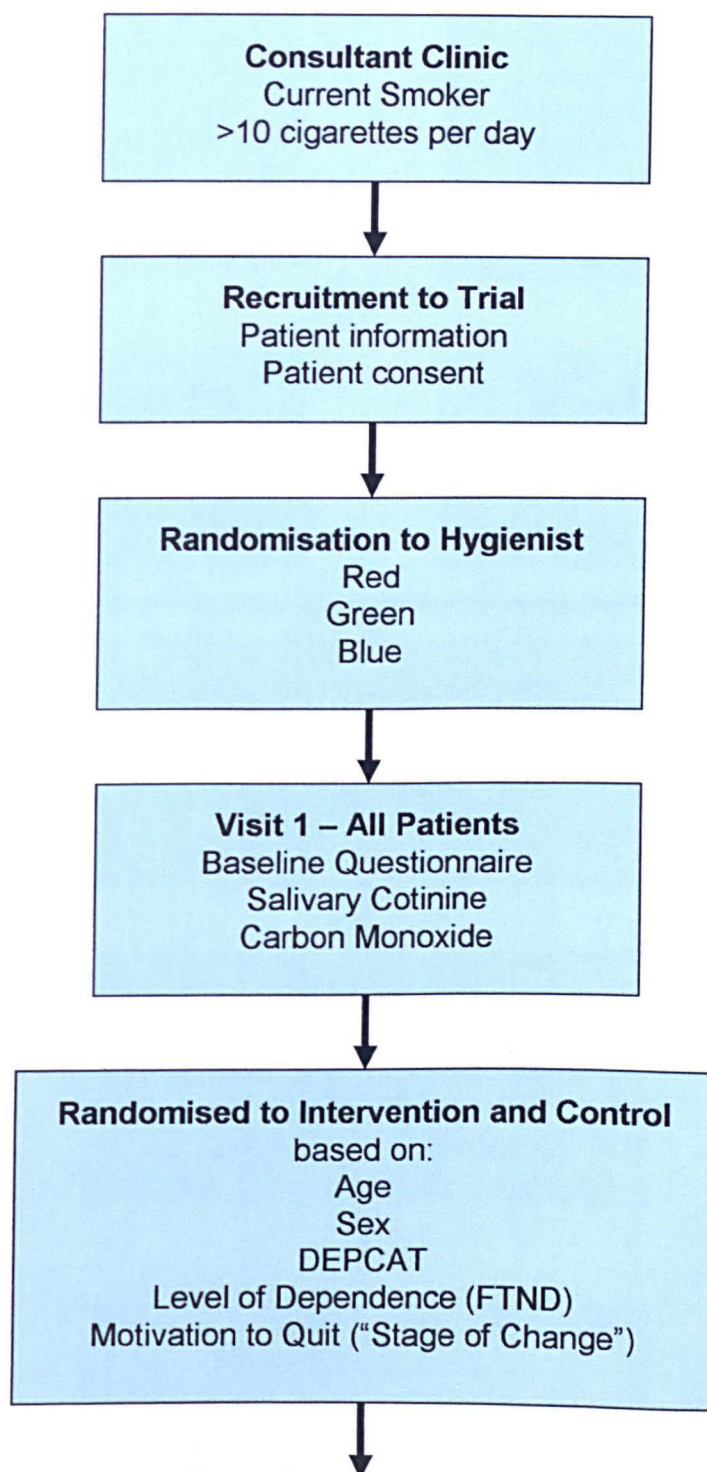
All statistical tests were considered to be statistically significant if the p-value was less than 0.05 and correspondingly if the confidence interval for the difference did not bracket zero.

3.3.16 Summary of Cessation Trial Methodology

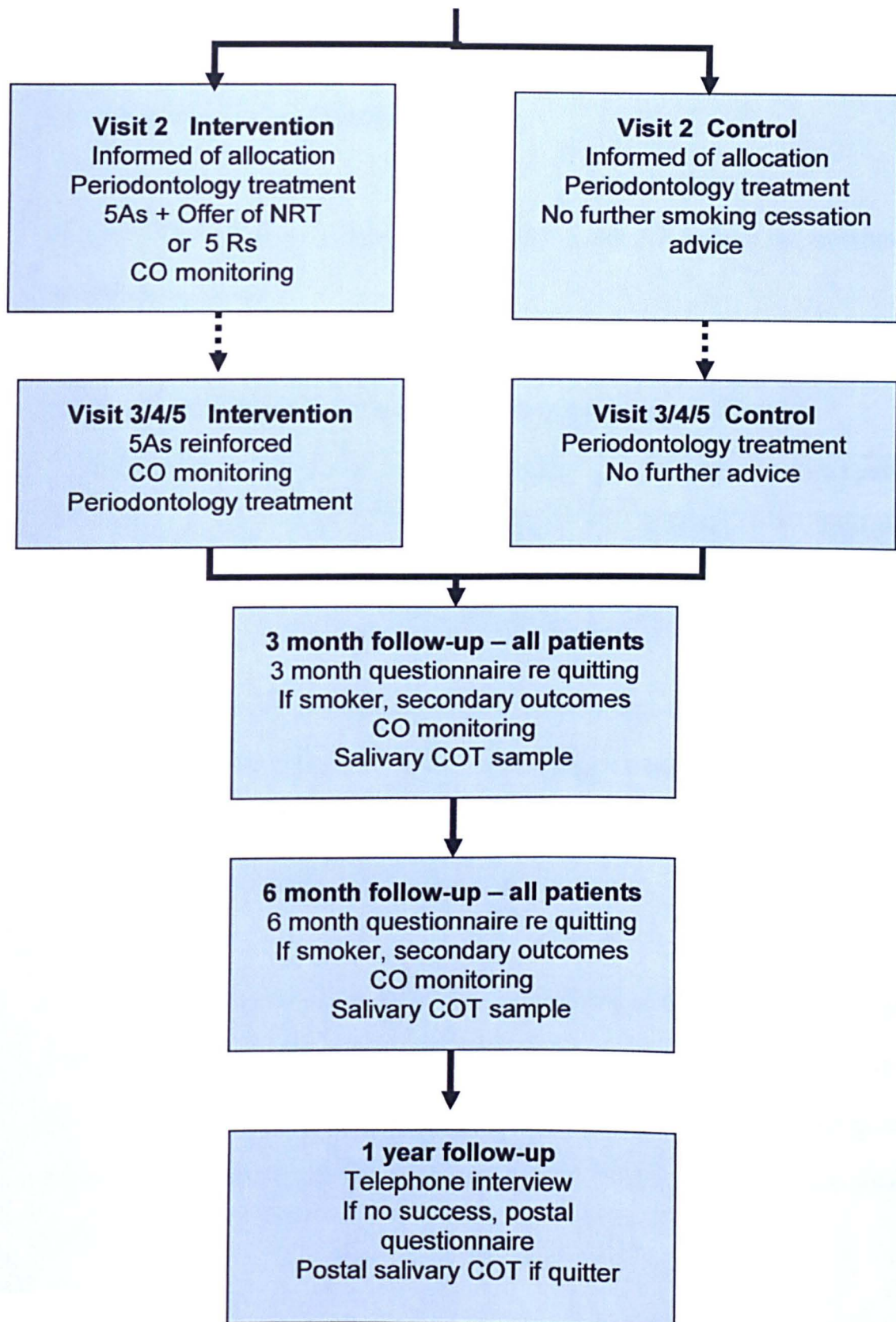
A diagrammatic summary of the stages of the smoking cessation trial is to be found in Figure 3.1 below.

Figure 3.1

SUMMARY OF SMOKING CESSATION TRIAL



SUMMARY OF SMOKING CESSATION (cont).



3.4 Baseline Results

3.4.1 Recruitment Phase

The patient recruitment phase began in April 2001 and lasted for 16 months, with the last patient enrolled into the trial in July 2002.

In total, 118 patients were recruited at baseline. Table 3.3 outlines the recruitment of patients by hygienist.

Table 3.3 Allocation of Recruited Patients by Hygienist and Group

Hygienist	No. Sessions Per Week	Intervention	Control	Total patients
Blue	9	23 (39%)	24 (41%)	47 (40%)
Red	8	21 (36%)	20 (34%)	41 (35%)
Green	5	15 (25%)	15 (25%)	30 (25%)
Total		59 (50%)	59 (50%)	118 (100%)

There was an unequal distribution of participants among the three hygienists which broadly reflected the number of sessions each hygienist worked per week, and thus their patient caseload. The 0.9 wte hygienist had 40% of the participants, while the 0.5 wte hygienist was responsible for 25% of the total recruited.

Following recruitment to the trial, one patient subsequently died, and one patient withdrew consent for follow-up visits; these two cases were therefore withdrawn from any further analysis. These participants had both been allocated to the control group.

Patient data collection was completed in July 2003. Therefore, the duration of the trial was 28 months.

3.4.2 Patient Characteristics

3.4.2.1 Gender of Participants

As can be seen from Table 3.4, there was an excess of females (71%) compared to males (29%) participating in the trial. There were slightly more males in the control group (35%) than intervention (24%). However, this difference was not statistically significant.

Table 3.4 Gender of Participants

	Intervention	Control	All
Male	14 (24%)	20 (35%)	34 (29%)
Female	45 (76%)	37 (65%)	82 (71%)
Total	59	57	116
$\chi^2 = 1.805, df = 1, p = 0.179$			

3.4.2.2 Deprivation Category of Participants

All deprivation categories were represented among participants recruited into the trial (Table 3.5). The majority of participants were from DEPCAT 4 (26 participants), with the lowest proportion from DEPCAT 1 (5 participants).

When looking at the differences between intervention and control groups, it can be seen that there were approximately equivalent numbers in each deprivation category, with the exception of DEPCAT 7 (21% control, compared to 8% intervention). Overall, there were no statistically significant differences between the numbers of participants in the intervention and control groups.

Table 3.5 Deprivation Category of Intervention and Control Groups

DEPCAT	Intervention	Control	All
1	3 (5%)	2 (3%)	5 (4%)
2	6 (10%)	6 (10%)	12 (10%)
3	7 (12%)	9 (16%)	16 (14%)
4	15 (25%)	11 (19%)	26 (22%)
5	10 (17%)	8 (14%)	18 (16%)
6	13 (23%)	9 (16%)	22 (19%)
7	5 (8%)	12 (21%)	17 (15%)
Total	59	57	116
$\chi^2 = 4.864, df = 6, p = 0.561$			

3.4.2.3 Age of Participants

As shown in Table 3.6, the youngest participant recruited was 22 years of age and the oldest 71. The mean age of the control group was statistically significantly higher than the intervention group by 3.6 years.

Table 3.6 Age of Participants

Age (Years)	All n=116	Intervention n=59	Control n=57	p-value	95% CI (C-I)
Mean (stdev)	41.2 (8.2)	39.9 (8.0)	43.5 (8.0)	0.019	(0.6, 6.5)
Range	(22–71)	(22–57)	(30–71)		

3.4.2.4 Nicotine Dependence Measures

A number of questions were asked about current tobacco usage to enable calculation of the Heaviness of Smoking Index, Fagerstrom Test for Nicotine Dependence and Fagerstrom Tolerance Test.

a) Daily Consumption of Cigarettes

Overall, the majority of trial participants (57%) smoked between 11 and 20 cigarettes per day (Table 3.7). One in ten smoked 10 cigarettes, with just under one-third of participants smoking 21 or more cigarettes per day. There was no statistical difference between the intervention and control groups with respect to number of cigarettes smoked.

Table 3.7 Participants' Reported Number of Cigarettes per Day, at Baseline

No. of cigarettes	Intervention	Control	All
10 or less	9 (15%)	4 (7%)	13 (11%)
11 - 20	33 (56%)	33 (58%)	66 (57%)
21 - 30	14 (24%)	17 (30%)	31 (27%)
31+	3 (5%)	3 (5%)	6 (5%)
Total	59	57	116
$\chi^2 = 2.18, df = 3, p = 0.536$			

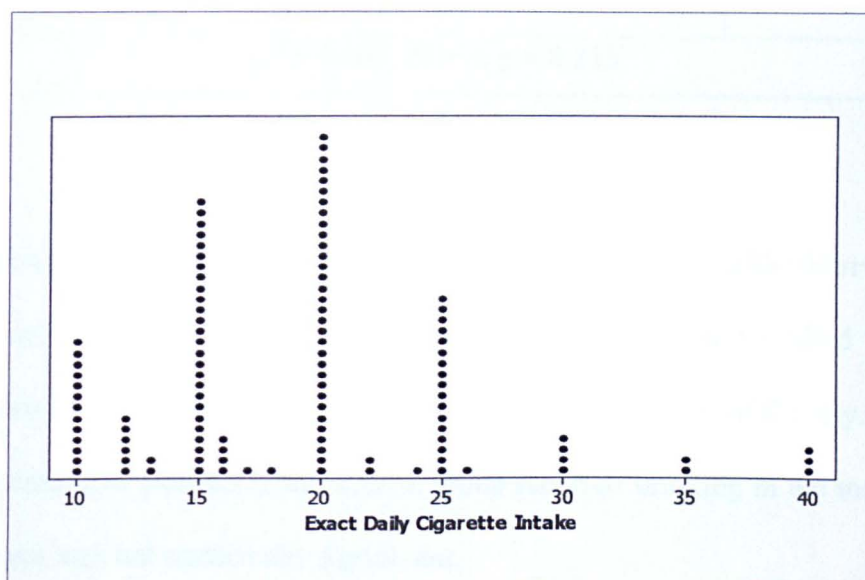
In response to the question about the exact amount smoked daily, Table 3.8 shows that the median number of daily cigarettes smoked was 20, i.e. a pack per day. This average level of smoking was the same for intervention and control groups.

Table 3.8 Participants' Reported Exact Daily Number of Cigarettes, at Baseline

	All n=116	Intervention n=59	Control n=57	p-value	95% CI (C-I)
Median	20	20	20	0.196	(-1, 5)
IQ Range	15-22	15-20	15-25		
Range	10-40	10-40	10-40		

With regard to the distribution of reported exact daily number of cigarettes for all participants, as illustrated in Figure 3.2, there is clumping of the data at 10, 15, 20 and 25 cigarettes per day.

Figure 3.2 All Participants' Self-Reported Exact Number of Cigarettes Smoked per Day at Baseline



b) Self-Reported Time to First Cigarette of the Day

Table 3.9 shows that few trial participants (7%) smoked within the first five minutes of waking, with the majority of participants smoking their first cigarette between 30 minutes and one hour after waking (52%). There was no significant difference between the intervention and control groups with regard to time taken to light up in the morning.

Table 3.9 Participants' Self-Reported Time to First Cigarette of the Day, at Baseline

	Intervention	Control	All
Less than 5 min	5 (9%)	3 (5%)	8 (7%)
6-30 min	4 (7%)	8 (14%)	12 (10%)
31-60 min	35 (59%)	25 (44%)	60 (52%)
Above 60 min	15 (25%)	21 (37%)	36 (31%)
Total	59	57	116
$\chi^2 = 4.467$, df = 3, p = 0.215			

c) Participants' Self-Reported Smoking more Frequently in the Morning

As can be seen in Table 3.10, a larger proportion of participants recruited to the trial smoked more frequently in the morning (57%) than at other times of the day. A slightly higher percentage of patients in the control group reported smoking in the morning, but this difference was not statistically significant.

Table 3.10 Participants' Self-Reported Smoking More Frequently in the Morning, at Baseline

	Intervention	Control	All
Yes	30 (51%)	36 (63%)	66 (57%)
No	29 (49%)	21 (37%)	50 (43%)
Total	59	57	116
$\chi^2 = 1.792$, df = 1, p = 0.181			

d) Difficulty in Refraining from Smoking in Public Places

Most participants in the trial, as can be seen in Table 3.11, did not find it difficult to refrain from smoking in public places, with no significant differences found between allocated groups.

Table 3.11 Participants' Self-Reported Difficulty in Refraining from Smoking in Public Places, at Baseline

	Intervention	Control	All
Yes	17 (29%)	10 (18%)	27 (23%)
No	42 (71%)	47 (82%)	89 (77%)
Total	59	57	116
$\chi^2 = 2.062, df=1, p = 0.151$			

e) Participants' Self-Reported Difficulty in Giving up First Cigarette of the Day

The majority (62%) of trial participants stated that they would find it difficult to give up their first cigarette of the day (Table 3.12). There was no significant difference between intervention and control groups.

Table 3.12 Participants' Self-Reported Difficulty in Giving Up First Cigarette of the Day, at Baseline

	Intervention	Control	All
Yes	38 (64%)	34 (60%)	72 (62%)
No	21 (36%)	23 (40%)	44 (38%)
Total	59	57	116
$\chi^2 = 0.279, df=1, p = 0.598$			

f) Participants' Self-Reported Smoking Habits when Ill in Bed

Most participants (75%) did not smoke in bed when ill (Table 3.13). There was no significant difference between intervention and control groups.

Table 3.13 Participants' Self-Reported Smoking Habits when Ill in Bed, at Baseline

	Intervention	Control	All
Yes	12 (20%)	17 (30%)	29 (25%)
No	47 (80%)	40 (70%)	87 (75%)
Total	59	57	116
$\chi^2 = 1.391, df=1, p = 0.238$			

g) Participants' Self-Reported Level of Nicotine in Cigarettes Smoked

As shown in Table 3.14, the majority of participants (64%) smoked cigarettes containing a medium level of nicotine, while one in three reported smoking low nicotine cigarettes. There was no statistically significant difference between the two groups.

Table 3.14 Participants' Self-Reported Level of Nicotine in Cigarettes Smoked, at Baseline

	Intervention	Control	All
Low nicotine	16 (28%)	18 (32%)	34 (30%)
Medium nicotine	38 (67%)	35 (61%)	73 (64%)
High nicotine	3 (5%)	4 (7%)	7 (6%)
Total	57	57	114
$\chi^2 = 0.384, df = 2, p = 0.825$			

h) Participants' Self-Reported Inhalational Smoking Habits

Table 3.15 shows that the majority of trial participants always inhaled cigarette smoke (92%). None of the subjects did not inhale at all. There was no statistically significant difference between the intervention and control groups with regard to this habit.

Table 3.15 Participants' Self-Reported Level of Inhalation of Cigarette Smoke, at Baseline

	Intervention	Control	All
Don't inhale	0 (0%)	0 (0%)	0 (0%)
Sometimes inhale	5 (9%)	4 (7%)	9 (8%)
Always inhale	52 (91%)	53 (93%)	105 (92%)
Total	57	57	114
$\chi^2 = 0.121, df = 1, p = 0.728$			

3.4.2.5 Composite Measures of Smoking Dependence

a) Heaviness of Smoking Index (HSI)

The HSI is a composite score based on two questions: the first with regard to number of cigarettes per day and the second alluding to 'time to first cigarette' of the day. The minimum achievable HSI is zero, and the maximum is six.

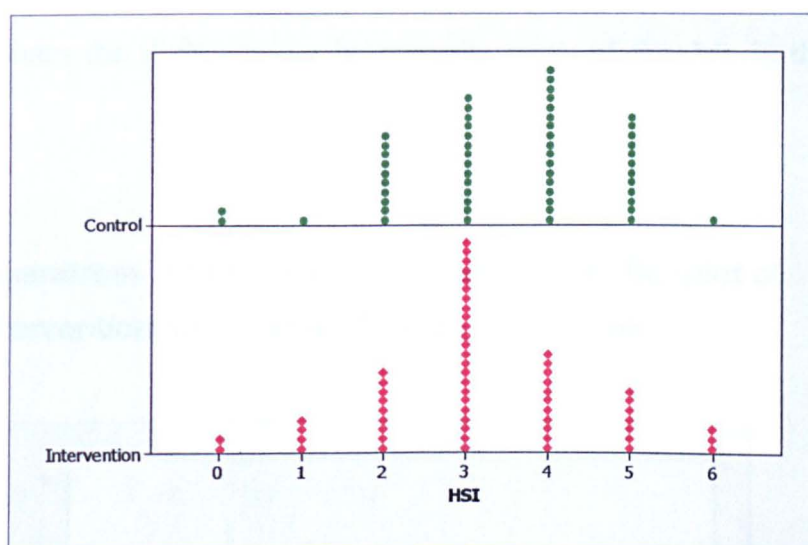
Table 3.16 shows that overall the HSI ranged from zero to six, with a median value of three for the intervention group and four for the control group. There was no statistically significant difference between the two groups.

Table 3.16 Heaviness of Smoking Index for Participants, at Baseline

	All n=116	Intervention n=59	Control n=57	p-value	95% CI (C-I)
Median	3.0	3.0	4.0	0.197	(0.0, 1.0)
IQ	3.0- 4.0	3.0-4.0	3.0-4.0		
Range	0-6	0-6	0-6		

Figure 3.3 illustrates the similar distributions of the HSI in the intervention and control groups.

Figure 3.3 Dotplot of Intervention and Control HSI scores, at Baseline



b) Fagerstrom Test for Nicotine Dependence

The Fagerstrom Test for Nicotine Dependence (FTND) comprises the two questions utilised in the Heaviness of Smoking Index, with an additional four questions relating to giving up the first cigarette of the day, smoking in public places, smoking when ill and smoking more in the morning. The minimum score in this index is zero, with a maximum score of 10.

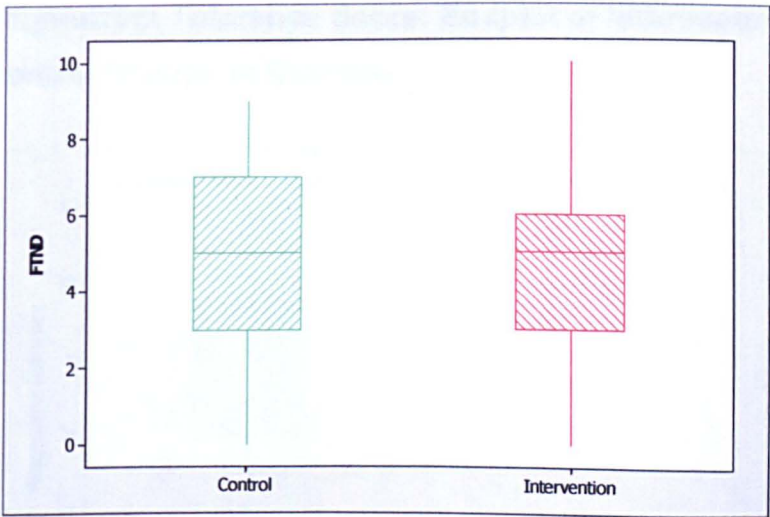
Table 3.17 indicates that the median value across all participants was five, with scores ranging from zero to 10. When the FTND scores of the two groups were compared, there was no statistically significant difference.

Table 3.17 Fagerstrom Test for Nicotine Dependence for Participants, at Baseline

	All n=116	Intervention n=59	Control n=57	p-value	95% CI (C-I)
Median	5.0	5.0	5.0	0.343	(0.0, 1.0)
IQ	3-6	3-6	3-7		
Range	0-10	0-10	0-9		

Figure 3.4 illustrates the slightly wider interquartile range of the data in the control group.

Figure 3.4 Fagerstrom Test for Nicotine Dependence: Boxplot of Intervention and Control Groups at Baseline



c) Fagerstrom Tolerance Score

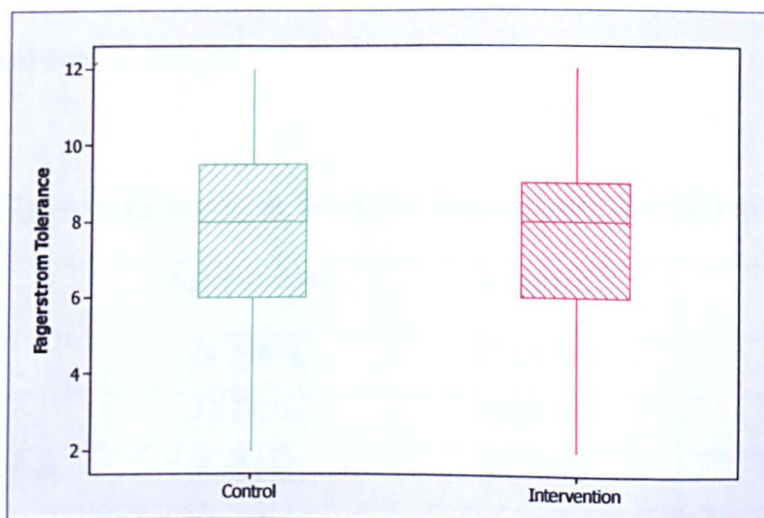
The Fagerstrom Tolerance Score includes data from the FTND and is supplemented by information relating to nicotine level in the cigarettes and inhalational habits. Almost the full range was used, with values ranging from two to 12 (the maximum value) being reported (Table 3.18). The median score was eight. There was no statistically significant difference between intervention and control groups.

Table 3.18 Fagerstrom Tolerance Score for Participants, at Baseline

	All n=115	Intervention n=58	Control n=57	p-value	95% CI (C-I)
Median	8.0	8.0	8.0	0.418	(-1.0, 1.0)
IQ	6.0-9.0	6.0-9.0	6.0-9.5		
Range	2.0-12.0	2.0-12.0	2.0-12.0		

As can be seen from Figure 3.5, there was a slightly wider interquartile range in the control group as compared to the intervention group.

Figure 3.5 Fagerstrom Tolerance Score: Boxplot of Intervention and Control Groups at Baseline



3.4.2.6 Environmental Exposure to Smoke

a) Exposure to Smoke at Home

Table 3.19 shows that the majority of trial participants were not exposed to smoke at home (61%). There was no statistically significant difference between the intervention and control groups.

Table 3.19 Exposure to Smoke at Home for Participants, at Baseline

	Intervention	Control	All
Yes	20 (34%)	25 (44%)	45 (39%)
No	38 (66%)	32 (56%)	70 (61%)
Total	58	57	115
$\chi^2 = 1.061, df = 1, p = 0.303$			

b) Exposure to Smoke at Work

Just over half (52%) of the trial participants reported being exposed to smoke at work (Table 3.20). Overall, 12% were not in paid employment, and hence experienced no workplace exposure. There was no statistically significant difference between the intervention and control groups.

Table 3.20 Exposure to Smoke at Work for Participants, at Baseline

	Intervention	Control	All
Yes	32 (56%)	27 (47%)	59 (52%)
No	19 (33%)	22 (39%)	41 (36%)
Not applicable	6 (11%)	8 (14%)	14 (12%)
Total	57	57	114
$\chi^2 = 0.929, df = 2, p = 0.628$			

3.4.2.7 Lifetime Measures of Smoking Exposure

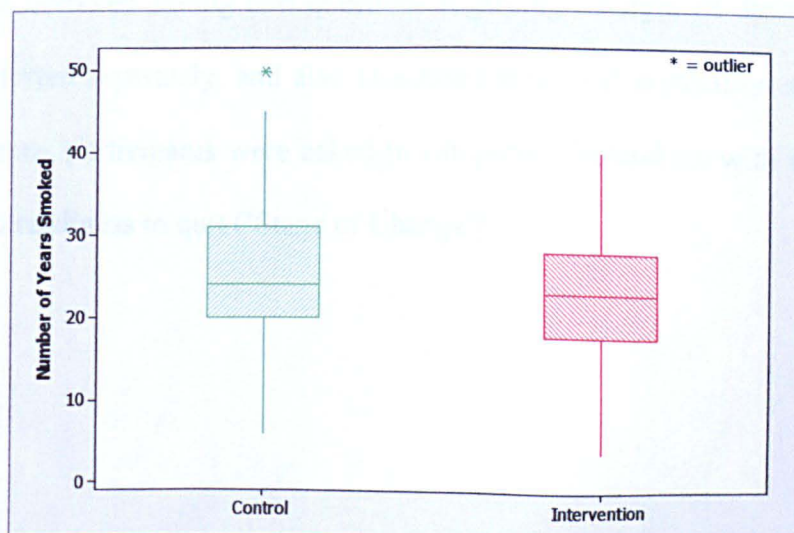
a) Number of Years Smoked

The trial participants were asked to recall the length of time they had been smokers. As shown in Table 3.21, the mean number of years smoked was slightly higher in the control group. However, the difference between intervention and control groups was not statistically significant. The smallest number of years smoked by a trial participant was four years, with the maximum reported number of years of smoking exposure being 50 years. It can be seen from Figure 3.6 that the range of the data for the control group was slightly wider. The boxplots also illustrate the slightly higher average number of years smoked for participants in the control group, compared to the intervention group.

Table 3.21 Number of Years Smoked by Participants, at Baseline

	All n=115	Intervention n=58	Control n=57	p-value	95% CI (C-I)
Mean (stdev)	23.8 (8.1)	22.5 (7.9)	25.2 (8.2)	0.08	(-0.3, 5.6)
Range	(4-50)	(4-40)	(6-50)		

Figure 3.6 Boxplot of Number of Years Smoked by Intervention and Control Groups, at Baseline



b) Pack-Years

Whole life exposure was calculated by multiplying the number of years smoked by number of packs of cigarettes (estimated at 20 cigarettes in a pack) per day, to give a self-reported measure of exposure.

There was a difference of 3.3 years in the mean number of pack-years between intervention and control, with the control group having the slightly higher exposure (Table 3.22). However, this difference was not statistically significant. The pack-years exposure of the participants ranged from 2 to 74 years.

Table 3.22 Number of Pack-Years for Participants, at Baseline

	All n=113	Intervention n=57	Control n=56	p-value	95% CI (C-I)
Mean (stdev)	23.1 (12.5)	21.5 (12.5)	24.8 (12.1)	0.16	(-1.3, 8.0)
Range	(2-74)	(2-74)	(3-64)		

3.4.2.8 Measures of Motivation to Quit

Two measures of motivation were used to determine the participants desire to quit. The first measure involved asking two questions regarding strength of desire to quit, and these are reported separately, and also as a composite total motivation score. For the second measure, participants were asked to categorise themselves with regard to their intention and readiness to quit ('Stage of Change').

a) Participants Desire to Stop Altogether, if They Could Do So Easily

Table 3.23 shows that the vast majority (90%) of trial participants would either definitely or probably quit if it was easy to do so. There was no difference between intervention and control groups.

Table 3.23 Participants' Self-Reported Desire to Stop Smoking, if they Could Do So Easily, at Baseline

	Intervention	Control	All
Yes, definitely	45 (78%)	46 (81%)	91 (79%)
Yes, probably	6 (10%)	7 (12%)	13 (11%)
Possibly	6 (10%)	3 (5%)	9 (8%)
Probably not	0 (0%)	1 (2%)	1 (1%)
Definitely not	1 (2%)	0 (0%)	1 (1%)
Total	58	57	115
$\chi^2 = 3.079, df = 4, p = 0.619$			

b) Participants' Desire to Stop Altogether

In response to the question about how much they wanted to stop altogether, 78% of participants said that they either strongly or quite strongly wanted to stop altogether (Table 3.24). There was evidence of an association between the group and the level of the desire to stop altogether. There were more control than intervention participants who responded that they very strongly wanted to stop altogether. There were more intervention than control participants who indicated that they moderately wanted to stop altogether.

Table 3.24 Participants' Self-Reported Desire to Stop Altogether, at Baseline

	Intervention	Control	All
Very strongly	19 (33%)	24 (42%)	43 (37%)
Quite strongly	22 (38%)	25 (44%)	47 (41%)
Moderately	15 (27%)	4 (7%)	19 (17%)
Slightly	2 (3%)	2 (4%)	4 (3%)
Not at all	0 (0%)	2 (4%)	2 (2%)
Total	58	57	115
$\chi^2 = 9.133$, $df = 4$, $p = 0.042$			

c) Total Motivation Score

It can be seen from Table 3.25, that the predominance of the measurements for the composite motivation scores are in the seven to eight range, with 71% of the participants having one of these scores.

Table 3.25 Distribution of Total Motivation Score for Participants, at Baseline

	Intervention	Control	All
2	0 (0%)	2 (0%)	2 (2%)
3	1 (2%)	1 (2%)	2 (2%)
4	6 (11%)	2 (3%)	8 (7%)
5	4 (7%)	2 (3%)	6 (5%)
6	11 (19%)	5 (9%)	16 (13%)
7	17 (30%)	22 (38%)	39 (34%)
8	19 (33%)	23 (40%)	42 (37%)
Total	58	57	115

The median motivation score for all participants was seven. There was no statistically significant difference between the intervention and control groups (Table 3.26).

Table 3.26 Total Motivation Score for Participants, at Baseline

	All n=115	Intervention n=58	Control n=57	p-value	95% CI (I-C)
Median	7	7	7	0.156	(0.0, 1.0)
IQ	6-8	6-8	6-8		
Range	2-8	3-8	2-8		

d) Measurement of ‘Stage of Change’

Table 3.27 indicates that only 13% of the trial participants were not interested in stopping and thus could be considered ‘contented smokers’. With regard to showing interest in stopping some time in the next six months, 45% of individuals reported to be in the category of ‘concerned smoker’, while 42% of participants reported wanting to stop within the next month.

Slightly more participants in the intervention group (46%) wanted to stop, compared to 38% in the control group, and there were more participants (16%) in the control group who were not interested in quitting compared to the intervention (10%). However, there was no statistically significance difference between the intervention and control groups with regard to the ‘Stage of Change’ of participants.

Table 3.27 ‘Stage of Change’ of All Participants, at Baseline

	Intervention	Control	All
Not interested (‘precontemplators’)	6 (10%)	9 (16%)	15 (13%)
Concerned (‘contemplators’)	26 (44%)	26 (46%)	52 (45%)
Want to stop (‘preparation’)	27 (46%)	22 (38%)	49 (42%)
Total	59	57	116
$\chi^2=1.076$, df = 2, p = 0.584			

3.4.2.9 Participants' Self-Reported Reasons for Wanting to Quit, at Baseline

Table 3.28 shows that the most popular reason for wanting to quit was a concern for health (95%), followed by the expense (80%). Only 50% had concerns about other people's exposure to smoke.

Table 3.28 Self-Reported Reasons for Wanting to Quit: All Participants, at Baseline

Health reasons	104 (95%)
Expense	92 (80%)
Don't like being addicted	66 (57%)
Not fair on other people	57 (50%)
Other reasons	25 (22%)
	Number replying = 115

3.4.2.10 Participants' Self-Reported Biggest Problem in Trying to Quit

Of the 116 participants, 104 (90%) gave information on what they perceived to be their biggest problem in attempting to give up smoking.

Comments were analysed and a number of key themes emerged from the data.

Problems concerning withdrawal caused by nicotine dependence were mentioned by 30 of the participants, while non-nicotine dependence issues such as habit and enjoyment were thought to be the major problem by 31 of the individuals recruited to the trial.

Issues relating to weight control and body image emerged as problems for 9 of the participants, with social issues regarding the use of alcohol being cited as the key problem for 9 of the respondents. Lack of self-efficacy or fear of failure was reported by 9 of the trial participants.

Environmental exposure to tobacco from those around the smokers, either at work or in the home was cited as a problem by six respondents.

Only one respondent cited 'No problem!'

3.4.2.11 Biochemical Assessment of Exposure to Nicotine, at Baseline

Two biochemical measures were used to assess exposure to nicotine at baseline, a salivary sample for cotinine analysis and an exhaled air sample for carbon monoxide analysis.

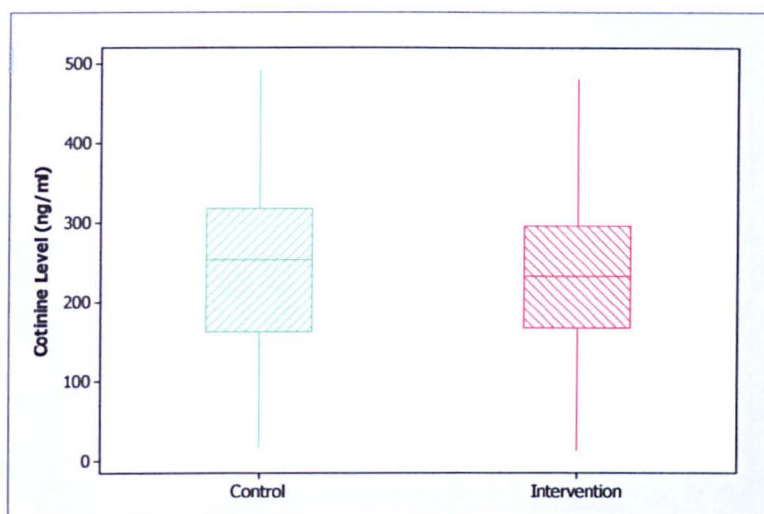
a) Measurement of Cotinine (COT)

As shown in Table 3.29, no statistically significant difference was seen between the intervention and control groups in terms of mean cotinine levels, with values of 232 and 243ng/ml respectively. However, there was a wide range in the levels of cotinine determined in the baseline samples. As can be seen from Figure 3.7, there was substantial overlap of the data for intervention and control groups, with the interquartile range of the control data being slightly wider.

Table 3.29 Levels of Salivary Cotinine (measured in ng/ml) of Participants, at Baseline

	All n=116	Intervention n=59	Control n=57	p-value	95% CI (C-I)
Mean (stdev)	237.5 (99.4)	231.9 (95.0)	243.3 (104.3)	0.539	(-25.3, 48.2)
Range	(14-491)	(14-479)	(18-491)		

Figure 3.7 Boxplot of Cotinine Levels in Intervention and Control Groups, at Baseline



b) Measurement of Carbon Monoxide (CO)

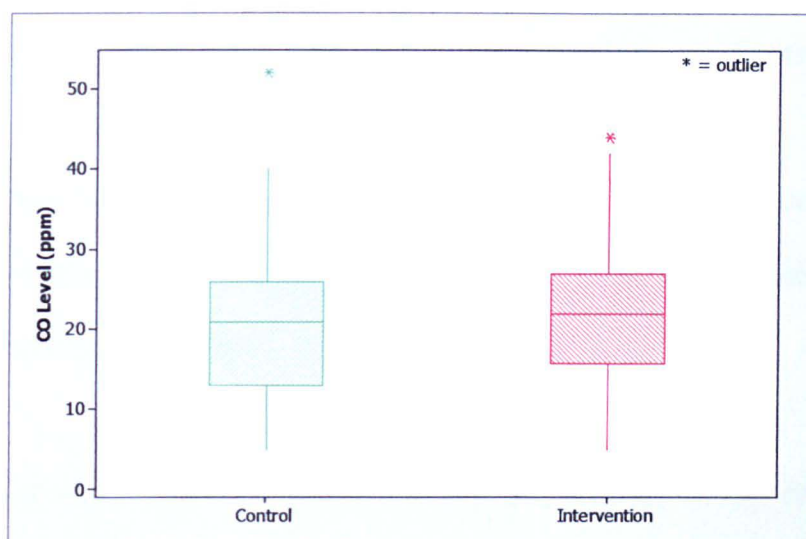
The mean carbon monoxide measurement (CO) in the intervention group was 22.0ppm compared to 20.8ppm in the control group (Table 3.30). This difference was not statistically significant. There was considerable variation in the baseline carbon monoxide measurements.

As can be seen from Figure 3.8, there was substantial overlap of the data, with an outlier in both the intervention and control groups. The CO level of 52ppm from a control participant would seem to be quite atypical.

Table 3.30 Levels of Carbon Monoxide (measured in parts per million) of Participants, at Baseline

	All n=112	Intervention n=58	Control n=54	p-value	95% CI (I-C)
Mean (stdev)	21.4 (8.9)	22.0 (8.8)	20.8 (9.1)	0.483	(-2.2, 4.5)
Range	(5.0-52.0)	(5.0-44.0)	(5.0-52.0)		

Figure 3.8 Boxplot of Carbon Monoxide levels in Intervention and Control Groups, at Baseline



3.4.2.12 Summary of Comparison of Control and Intervention Groups with respect to Randomisation Factors

The aim of the randomisation (as detailed in Section 3.3.8) was to provide balance between the intervention and control groups with respect to age, sex, DEPCAT, level of nicotine dependence and intention to quit as measured by ‘Stage of Change’.

There was no statistically significant difference between intervention and control groups with respect to sex and DEPCAT. Similarly, there was no difference between the intervention and control groups with respect to level of nicotine dependence, as measured by FTND and HSI, nor with regard to motivation to quit, as measured by ‘Stage of Change’ and Motivation Scores.

There was a difference with regards to age, with a statistically significantly higher mean age of 3.6 years in the control group. The 95% confidence interval suggests that the mean difference in age could be as little as 0.6 years or as high as 6.5 years.

As regards the biochemical measures of tobacco exposure, namely carbon monoxide (CO) and cotinine (COT), there were no statistically significant differences between intervention and control groups.

Therefore, the intervention and control groups participating within this randomised controlled trial were similar with respect to all baseline factors randomised on, with the one exception of age.

3.5 Three Month Outcomes

3.5.1 Patient Follow-ups

Three-month data were obtained from 102 of the 116 participants (88%) registered at baseline.

Table 3.31 shows the distribution of participants lost to the study in both the intervention and control groups. There were equal numbers of participants (seven) in each group for which it proved impossible to obtain follow-up data.

Table 3.31 Follow-up of Participants at 3 Months

	Number of Participants	
	Intervention (%)	Control (%)
At baseline	59 (51%)	57 (49%)
At 3 months	52 (88%)	50 (88%)
'Lost' to study at 3 months	7 (12%)	7 (12%)

Analysis of the 14 individuals lost to the trial indicated that, with regard to age, the mean for the intervention group was 41.9 (SD 5.6) years compared to 41.4 (SD 5.7) years in the control group. The median number of cigarettes smoked in the intervention and control groups at baseline were 20 (range 10-20) and 15 (range 10-20) per day, respectively. With regards to pack-years, the intervention group had a slightly higher mean exposure of 23.4 (SD 7.7) years compared to 18.0 (SD 7.5) years in the control group.

3.5.2 Number of Treatment Visits of Participants between Baseline and 3 Months

Information was collected on the number of visits to the hygienists by the participants for the time period between baseline and three months. The median number of visits for both groups was four, with ranges of one to six and two to seven for the intervention and control groups respectively.

3.5.3 Primary Outcome at 3 Months

3.5.3.1 Self-Reported Smoking Status at 3 Months

At three months, each participant was asked whether they considered themselves to be smoker. A summary of the responses is displayed in Table 3.32. It can be seen that nine (17%) of the participants in the intervention group described themselves as quitters, compared to five (10%) in the control group. However, the difference between intervention and control in terms of the proportion of participants reporting as having quit did not reach statistical significance ($p=0.484$, 95% CI (I-C)=(-9, 28)%).

Table 3.32 Participants' Self Reported Smoking at 3 Months

Are you a smoker?	Intervention	Control	All
No	9 (17%)	5 (10%)	14
Yes	43 (83%)	45 (90%)	88
Total	52	50	102

3.5.3.2 Summary of Self-Reported Quitters at 3 Months including

Biochemical Measures of Cotinine (COT) and Carbon Monoxide (CO)

In addition to the measure of self-report, two further measures of smoking cessation, both biochemical, were collected from patients. Additionally, information on exposure to NRT medication at the three month time period was collected. In Table 3.33, information regarding the 14 participants who claimed to have quit, including log number, allocated group, treating hygienist, level of COT and CO, and NRT use at time of sampling are displayed.

Table 3.33 Three Month Summary Table of Biochemical Measures (COT, CO) and use of NRT at Time of Sampling, for Self-Reported Quitters

Log	Allocated Group	Hygienist	COT (ng/ml)	CO (ppm)	NRT Use at time of sampling
1	I	Blue	<2	1	no
2	I	Green	<2	2	no
36	I	Red	28	2	no
50	I	Red	16	3	no
58	I	Red	71	20	no
81	I	Blue	111	5	Gum
83	I	Green	<2	1	no
86	I	Blue	<2	2	no
103	I	Blue	<2	1	no
21	C	Red	<2	2	no
43	C	Red	140	3	Patches
61	C	Green	33	3	no
82	C	Blue	17.5	-	Lozenges
118	C	Blue	106	8	Patches

The participants' log number gives an approximate timescale of when participants were recruited to the study. It can be seen there were two successful quitters early on in the trial, i.e. cases 1 and 2, and a clustering of participants enrolled in the 80's, i.e. 81, 82, 83 and 86.

All hygienists had participants who claimed to have quit, both in intervention and control groups. The Blue hygienist had four intervention and two control quitters. The Green hygienist had two intervention and one control, the Red hygienist had two intervention and two control participants who claimed to have stopped tobacco use.

With respect to CO measurements, 12 trial participants, (eight intervention, four control) had values of 8ppm or below. There was no measurement of CO for one individual (participant 82), and one person (participant 58) had a value of 20ppm, well above the cut-off.

With respect to cotinine levels, eight individuals (six intervention and two control) had values below the cut-off of 20ng/ml. Six individuals had levels above this, and these are detailed on a case-by-case basis below.

A number of the trial participants reported using NRT at the 3-month point (participants 43, 81, 82, 118). In the intervention group, one reported its usage and in the control group there were three participants who were taking this medication at the time cotinine sampling was undertaken. All had CO levels below the cut-off value of 9ppm.

Additionally, two cases had slightly higher cotinine levels than the previously stated cut-off point. Participant 36 had a cotinine of 28ng/ml and participant 61 had a cotinine of 33ng/ml. Both had low CO values below the cut-off level, 2 and 3ppm respectively. When notice is taken of the baseline measurements, participant 36 then had a cotinine level of 232ng/ml and CO of 15ppm. The level of COT at 3 months constituted an 88% drop in cotinine levels. For participant 61, the baseline measurements were COT 185ng/ml and CO 13ppm. The 3-month value constituted an 82% drop in cotinine levels.

One individual (participant 58) claimed to have quit, though cotinine and carbon monoxide levels were substantially above the cut-off (71ng/ml and 20ppm respectively). This subject reported no exposure to nicotine replacement therapy. The classification of a patient who reports non-smoking which is not corroborated by the biochemistry is a 'deceiver'.

In addition to those individuals who claimed to have quit, one trial participant (113) allocated to the intervention group (Blue hygienist) described themselves as a smoker, but had biochemistry more appropriate for a quitter. With a COT level of 18ng/ml and a CO of 2ppm, these values would indicate that this individual was more suitably categorised as a non-smoker. Such an individual can be classified as a 'closet quitter'.

3.5.3.3 Definitive Quitters as measured by Self-report, Cotinine and CO Analysis at 3 Months

Table 3.34 shows the definitive categorisation of smoking status, taking into account all available evidence. This resulted in 14 participants being classified as quitters.

Table 3.34 Definitive Quitters as measured by Self-Report, Cotinine and CO Analysis at 3 Months

Log Number	Allocated Group	Self Report	Cotinine	CO	Category
1	I	✓	✓	✓	quitter
2	I	✓	✓	✓	quitter
36	I	✓	✗	✓	quitter
50	I	✓	✓	✓	quitter
81	I	✓	✗	✓	quitter
83	I	✓	✓	✓	quitter
86	I	✓	✓	✓	quitter
103	I	✓	✓	✓	quitter
113	I	✗	✓	✓	closet quitter
21	C	✓	✓	✓	quitter
43	C	✓	✗	✓	quitter
61	C	✓	✗	✓	quitter
82	C	✓	✓	-	quitter
118	C	✓	✗	✓	quitter

Blue=Intervention Purple= Control

Therefore, in summary, with respect to all patients followed-up, there were nine participants (17.3%) who were classified as quitters in the intervention group, compared to five (10.0%) in the control group. There was no statistically significant difference between intervention and control groups in terms of the proportion of participants classified as quitters ($p=0.484$, 95% CI (I-C)=(-9.3, 27.9)%). However, the 95% CI for the difference does indicate that the difference could be as much as 28% in favour of intervention over control.

However, assuming all patients lost to follow-up were still smoking, the nine and five definitive quitters represented quit rates of 15.3% and 8.8% of the intervention and control patients recruited respectively. However, the difference between intervention and control groups, in terms of the proportion of participants defined as having quit, did not reach statistical significance ($p=0.449$, 95% CI (I-C)=(-8.4, 25.6)%).

3.5.3.4 Self-Reported Pharmacological Use in 3-Month Quitters

Although four of the quitters were using NRT at the 3-month time point, several others had employed this aid to smoking cessation during the preceding three months. Table 3.35 details the different types of nicotine replacement therapies used by the quitters in the trial during the previous three months.

Table 3.35 Use of Nicotine Replacement Therapy by Quitters during Initial 3 Month Period

Log	Allocation	Hygienist	NRT or Zyban use
1	I	Blue	Patches(Nic)
2	I	Green	Patches(Nic)
36	I	Red	Patches(Nic)
50	I	Red	nil
81	I	Blue	Gum(Nic)
83	I	Green	Lozenges(NQ)
86	I	Blue	nil
103	I	Blue	Patches(Nic)
113	I	Blue	nil
21	C	Red	Zyban
43	C	Red	Patches(N/elle)
61	C	Green	nil
82	C	Blue	Lozenges(NQ)
118	C	Blue	Patches(NQ)

Nic = Nicorette (brand of NRT in patches or gum form, provided free in trial)

N/elle = Nicotinelle

NQ = Niquitin

Most of the 3-month quitters reported using some form of NRT: five of the intervention group reported using Nicorette patches provided by the study, one used Nicorette gum (also provided) and one participant purchased NiQuitin lozenges. With regard to the control group, one patient used Zyban, one used Nicotinelle patches, one Niquitin patches and one used Niquitin lozenges. Three participants from the intervention group and one from the control group reported no use of pharmacological aids in quitting.

3.5.4 Secondary Outcomes at 3 Months

Those participants who classified themselves as smokers three months after recruitment, were asked a number of questions about possible changes in their smoking behaviour. Questions covered included details about attempts at quitting, as well as reduction in smoking and changing to a low tar brand. Excluded from the analysis below is the one

intervention participant who was classified as a quitter on the basis of biochemical measurements. In addition, data were not collected from the ‘deceiver’.

3.5.4.1 Self-Reported Attempts at Quitting

Participants were asked about whether they had had a quit attempt in the previous three months, and if so, how many. As can be seen from Table 3.36, 56% of the intervention group reported a quit attempt, compared to 43% of the control group. With respect to two or more quit attempts, one third (33%) of the intervention participants and 30% of the control group reported that they had tried to give up tobacco. Neither of these differences was statistically significant.

With regard to length of quit attempt, 55% of the intervention group and 39% of the control group had attempted to quit for 24 hours or more. This difference was not statistically significant. When asking participants about a longer and more sustained quit attempt of at least one week, 37% of the intervention group and 18% of the control group reported a quit attempt of this duration. This difference was statistically significant.

Table 3.36 Self Reported Quit Attempts (number and duration) of Participants at 3 Months

Quit attempts:	Number (%) of Participants Reporting Quit Attempts				
	All n=87	Intervention n=43	Control n=44	p-value	95% CI (I-C)
In last 3 months	43 (49%)	24 (56%)	19 (43%)	0.235	(-8, 34)%
2 or more	27 (31%)	14 (33%)	13 (30%)	0.761	(-16, 23)%
24 hours or more*	40 (47%)	23 (55%)	17 (39%)	0.129	(-5, 37)%
1 week or more	24 (28%)	16 (37%)	8 (18%)	0.043	(1, 37)%

*This question was answered by 86 participants (42 Intervention, 44 Control)

3.5.4.2 Use of Nicotine Replacement Therapy in Participants Categorised as Non-Quitters at 3 Months

With respect to the use of NRT in trial participants in the intervention group who were not categorised as quitters at 3 months, 15 tried patches and 9 used gum.

No data were available on NRT use in the control group who did not report quitting at 3 months.

3.5.4.3 Changes in Smoking Behaviours

Information was elicited relating to a number of other areas of behaviour related to smoking.

Table 3.37 shows that a high number of intervention (93%) and control (86%) patients delayed smoking for greater than 5 minutes after waking. Few participants reported trying to modify their smoking behaviour by inhaling less of the cigarette smoke, with only 28% of the intervention group and 18% of the control group adopting this behaviour. With regard to smoking less of a cigarette, 56% of the intervention group took this action, compared to 45% of the control group. When asked about brand changing and switching to a low tar cigarette, 28% of the intervention group self-reportedly did this, compared to 16% of the control group.

There were no statistically significant differences with respect to any of the above changes in smoking behaviour, although the 95% confidence intervals are wide, and there is some evidence of the intervention groups performing better than those in the control group.

With respect to number of cigarettes smoked, 81% of the intervention group reported they had reduced their intake, compared to 45% of the controls. This difference was of statistical significance ($p < 0.001$).

Table 3.37 Self-reported Changes in Smoking Behaviour at 3 Months

	Number (%) of Participants				
	All n=87	Intervention n=43	Control n=44	p-value	95% CI (I-C)
Delay Smoking for >5 min	78 (90%)	40 (93%)	38 (86%)	0.303	(-6, 19)%
Inhale Less of a Cigarette	21 (24%)	12 (28%)	9 (18%)	0.415	(-11, 25)%
Smoke Less of a Cigarette	44 (51%)	24 (56%)	20 (45%)	0.331	(-11, 31)%
Changed to Low Tar Cigarettes	19 (22%)	12 (28%)	7 (16%)	0.172	(-5, 29)%
Reduced Number of Cigarettes per Day	55 (63%)	35 (81%)	20 (45%)	<0.001	(17, 55)%

When examining the self-reported percentage reduction in daily number of cigarettes (Table 3.38), the median reduction was 33% for the intervention group and 0% for the control group. This difference was statistically significant.

Table 3.38 Percentage Self-Reported Reduction in Cigarette Intake at 3 Months

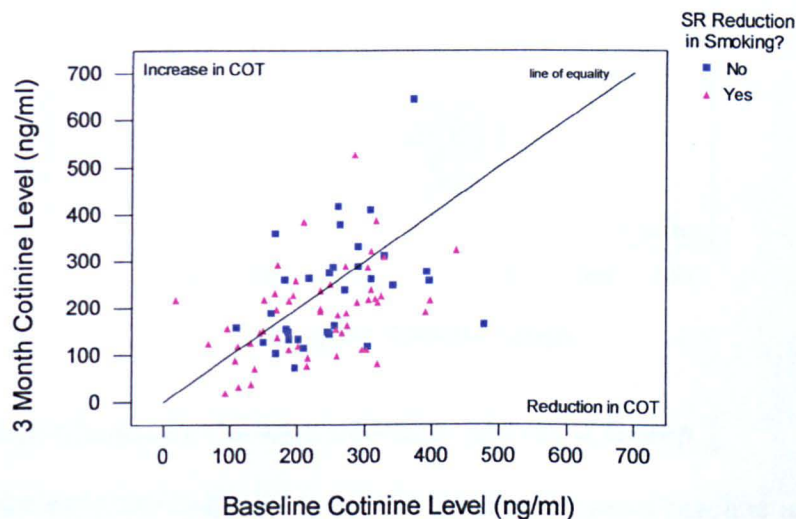
	All n=85	Intervention n=41	Control n=44	p-value	95% CI (I-C)
Median	25	33	0		
IQ Range	0-49	20-50	0-38		
Range	0-90	0-90	0-75		

3.5.4.4 Relationship of Self-Reported Smoking Reduction in Cigarettes and Cotinine Levels at Baseline and 3 Months for Individual Participants

Changes in cotinine measurements between baseline and 3 months were studied in relation to corresponding self-reported reductions in smoking levels.

Levels of cotinine at baseline and 3 months were plotted for those participants who reported either a reduction or no reduction in smoking (Figure 3.9). Those participants who reported having reduced, did not always have a concomitant reduction in cotinine levels.

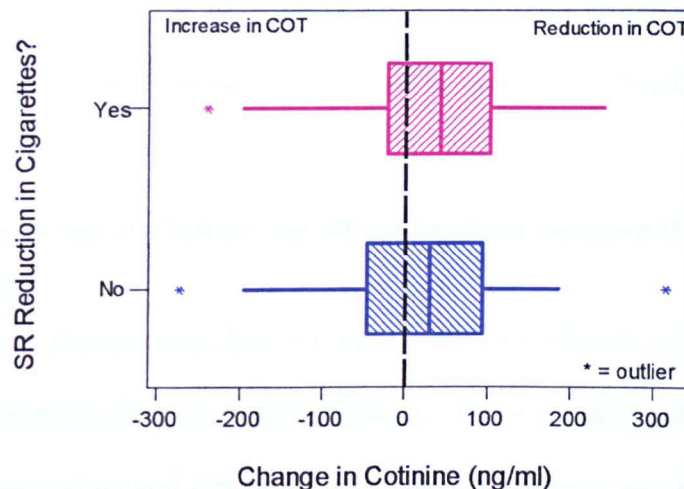
Figure 3.9 Relationship of Self-Reported Reduction in Cigarettes and Cotinine levels at Baseline and 3 Months for Individual Participants



3.5.4.5 Relationship of Reduction in Cotinine Levels between Baseline and 3 Months and Self-Reported Reduction in Cigarettes

Figure 3.10 uses a boxplot to illustrate the relationship of change in cotinine (baseline level minus 3 month level) and self-reported reduction in cigarettes. There was a slightly higher mean reduction in cotinine, 39 (SD 100)ng/ml in the group who did NOT report reducing their smoking (coded in blue), compared to a mean value of 18 (SD 115)ng/ml in the group who reported reducing (coded in pink) ($p=0.404$, 95% CI (C-I)=(-29,70)ng/ml).

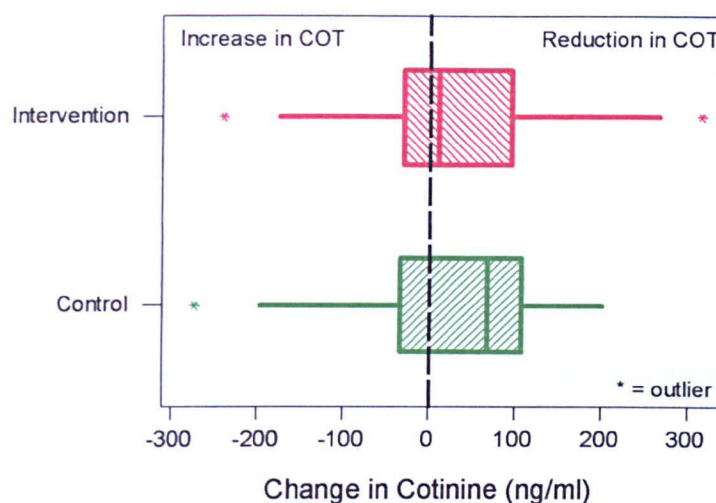
Figure 3.10 Boxplot of Change in Cotinine Levels and Self-Reported Reduction in Cigarettes at 3 Months



3.5.4.6 3-Month Change in Cotinine Levels by Allocated Group

Figure 3.11 illustrates the change in levels of cotinine between baseline and 3 months (baseline level minus 3 month level) in the two groups. A slightly higher mean reduction was seen in the control group (coded in green) (38 (SD 107)ng/ml), compared to the mean value of 29 (SD 111)ng/ml in the intervention group (coded in red). There was no statistically significant difference in the reduction of cotinine between the intervention and control groups ($p=0.713$, 95% CI (C-I)=(-38, 55)ng/ml).

Figure 3.11 Boxplot of Change in Cotinine Levels by Allocated Group at 3 Months



3.5.5 Changes in Intention to Stop Smoking at 3 Months

All participants were asked at baseline and at 3 months about whether they considered themselves to be 'contented smokers', 'concerned smokers' or 'wanting to stop'.

3.5.5.1 Shift in 'Stage of Change' for all Participants Between Baseline and 3 Months

Table 3.39 details the baseline data for all the trial participants and the 'stages' those participants self-reportedly held at three months. Those participants who made positive behaviour change and moved forward in the 'Cycle of Change' are coded in pink. Those participants for whom there was no change between baseline and 3 months are coded in blue. Some participants moved backwards in the cycle, i.e. reported being less likely to quit, and these are coded in green.

Table 3.39 shows that 29 trial participants moved forward, with 14 quitting and 15 reporting being more likely to quit at 3 months than at baseline. The majority of the trial participants (51) reported being in the same 'Stage of Change' at 3 months as they

had been at baseline. With regard to those who moved backwards in the cycle and reported being less likely to quit at 3 months, 20 individuals fitted this category.

Table 3.39 Shift in ‘Stage of Change’ for All Participants at 3 Months

Status at Baseline	Status at 3 Months			
	Contented	Concerned	Want to stop	Quitter
Contented	6	6	-	1
Concerned	1	31	9	4
Want to stop	1	18	14	9

No Change: blue

Positive Change: pink

Negative Change: green

3.5.5.2 Shift in ‘Stage of Change’ for Intervention Group at 3 Months

In Table 3.40, the position in the ‘Cycle of Change’ of the intervention participants at 3 months, relative to baseline, is shown. Fourteen individuals moved forward, and were more likely to quit at 3 months (coded in pink), while seven individuals moved backwards in the cycle (coded in green). Twenty eight of the participants were in the same ‘Stage of Change’ at 3 months as at baseline (coded in blue).

Table 3.40 Shift in ‘Stage of Change’ for Intervention Group at 3 Months

Status at Baseline	Status at 3 Months			
	Contented	Concerned	Want to stop	Quitter
Contented	2	3	-	-
Concerned	0	17	3	2
Want to stop	0	7	9	6

No Change: blue

Positive Change: pink

Negative Change: green

3.5.5.3 Shift in 'Stage of Change' for Control Group at 3 Months

In the control group, there were 12 participants who made negative changes in the cycle, 23 participants who stayed in the same place and 15 who moved forward in the 'Cycle of Change' (Table 3.41).

Table 3.41 Shift in 'Stage of Change' for Control Group at 3 Months

Status at Baseline	Status at 3 Months			
	Contented	Concerned	Want to stop	Quitter
Contented	4	3	-	1
Concerned	1	14	6	2
Want to stop	1	10	5	3

No Change: blue

Positive Change: pink

Negative Change: green

3.5.6 Number of Treatment Visits for Quitters and Non-Quitters at 3 Months

The median number of visits between baseline and three months for quitters was 4.5 (range 1-6), with the median number of visits for trial participants categorised as smokers at 3 months being 4.0 (range 2-7).

3.6 Six Month Outcomes

3.6.1 Patient Follow-ups

Six-month data were obtained from 71 (61%) of the 116 participants registered at baseline.

Table 3.42 shows the distribution of participants lost to the study in both the intervention and control groups.

Table 3.42 Follow-up of Participants at 6 Months

	Intervention	Control	Total
At baseline	59 (51%)	57 (49%)	100%
At 3 months	52 (88%)	50 (88%)	88%
At 6 months	36 (61%)	35 (61%)	61%
‘Lost’ to study at 6months	23 (39%)	22 (39%)	39%

Forty-five (39%) of the participants recruited at baseline were lost to follow-up at the 6 month time period. The fall out rates for the intervention and control groups were very similar, with 23 (39%) and 22 (39%) of the participants lost to the two groups respectively.

Of the 45 individuals for whom it proved impossible to obtain 6 month data, the mean age was 40.3 years (SD 6.3) in the intervention group, compared to 42.0 (SD 8.0) in the control group. The median number of cigarettes smoked in the intervention and control groups was 20 (range 10-35) and 20 (range 10-40) respectively. With regard to pack-years, the exposure in the control group was slightly higher with a mean value of 26.5 (SD 14.2) compared to 22.4 (SD 10.5) in the intervention group.

3.6.2 Number of Treatment Visits Between Baseline and 6 Months for All Participants

The number of visits to the hygienist was collected for both intervention and control groups. For the intervention group, the median number of visits, between 3 and 6 months, and baseline and 6 months, was 2 (range 0-5) and 6 (range 4-8) respectively. With regard to the control group, over the same time periods, the median number of visits was 2 (range 0-5) and 6 (range 3-8) respectively.

3.6.3 Primary Outcome at 6 Months

3.6.3.1 Self-Reported Smoking Status

At the six-month time point, participants were asked whether they considered themselves to be smokers. Table 3.43 shows that six participants (17%) in the intervention group and three (9%) in the control group described themselves as quitters.

Table 3.43 Participants' Self Reported Smoking at 6 Months

Are you a smoker?	Intervention	Control	All
No	6 (17%)	3 (9%)	9 (13%)
Yes	30 (83%)	32 (91%)	62 (87%)
Total	36	35	71

There was no statistically significant difference between intervention and control group in terms of the proportion of participants self-reported as having quit (p -value=0.485, 95% CI (I-C)=(-12, 34)%). It should be noted that the confidence interval is wide, and this interval may indicate a benefit in favour of the intervention group.

3.6.3.2 Summary of Self-Reported Quitters at 6 Months including

Biochemical Measures of Cotinine (COT) and Carbon Monoxide (CO)

The information collected at the 6-month time point, was similar to that collected at 3 months. Thus, in addition to self-reported measures recorded via questionnaires, samples of exhaled air and saliva were collected for CO and cotinine analysis respectively.

Table 3.44 summarises information from the trial participants who self-reported quitting and includes information on log number, allocated group, treating hygienist and biochemical measures of COT and CO, in addition to reported NRT use at time of sample collection.

Table 3.44 Six Month Summary Table of Biochemical Measures (COT, CO) and Use of NRT at Time of Sampling for Self-Reported Quitters

Log	Allocation	Hygienist	COT (ng/ml)	CO (ppm)	NRT Use at time of sampling
1	I	Blue	<2	1	no
2	I	Green	<2	2	no
39	I	Red	<2	2	no
60	I	Green	87	2	Patches (Nic)
83	I	Green	5.2	2	no
103	I	Blue	<2	2	no
21	C	Red	<2	1	no
43	C	Red	<2	-	no
118	C	Blue	38	1	Patches (NQ)

Nic= Nicorette (brand of NRT in patches or gum form, provided free in trial)

N/elle = Nicotinelles

NQ = Niquitin

All hygienists had participants who claimed to have quit, both in the intervention and control groups. The Blue hygienist had two intervention and one control patient, the Green hygienist had three intervention patients and the Red hygienist had one intervention and two control patients who stopped smoking.

One participant in each group claimed to be using NRT at the time of cotinine sampling (participants 60 and 118). Both had cotinine levels above the 20ng/ml cut-off, but low CO values.

3.6.3.3 Definitive Quitters as measured by Self-Report, Cotinine and CO Analysis at 6 Months

Table 3.45 shows the categorisation of smoking status, taking into account all available evidence. The self-reporting quitters were all definitely classified as non-smokers, six intervention (16.7%) and three controls (8.6%). The use of biochemical validation did not change the classification of any of the participants' smoking status compared to the self-report.

Table 3.45 Definitive Quitters as measured by Self-Report, Cotinine and CO analysis at 6 Months

Log Number	Self Report	Cotinine	CO	Category
1	✓	✓	✓	quitter
2	✓	✓	✓	quitter
39	✓	✓	✓	quitter
60	✓	✗	✓	quitter
83	✓	✓	✓	quitter
103	✓	✓	✓	quitter
21	✓	✓	✓	quitter
43	✓	✓	-	quitter
118	✓	✗	✓	quitter

Blue=Intervention Purple= Control

Of the patients recruited at baseline, 6 (10.2%) in the intervention group were definitive quitters, compared to 3 (5.3%) in the control group. However, there was no significant difference between intervention and control group in terms of the proportion of participants self-reported as having quit (p-value=0.530, 95% CI (I-C)=(-8.5, 23.6)%).

3.6.3.4 Prolonged Abstinence Measures at 6 Months

With respect to prolonged abstinence measures, four of the intervention and three of the control were biochemically validated as quitters at 3 months (participant numbers 1, 2, 83, 103, 114, 118).

Of patients followed-up, prolonged abstinence measures would indicate that 11.1% in the intervention group had quit compared to 8.6% in the control group.

When prolonged abstinence is considered in terms of all patients recruited to the study, the corresponding figures are 6.8% for the intervention group and 5.3% for the control group.

3.6.3.5 Characteristics of Six Month Quitters

As can be seen from Table 3.46 below, all of the quitters at 6 months were female. With respect to age, in the intervention group, five (out of six) were aged 37 or younger, with one quitter aged 53. In the control group, there was one participant in each of the mid-life decades (32, 49, 54).

With respect to DEPCAT, in the intervention group, five (out of six) were in the more affluent DEPCAT 1-4, with one participant (103), from DEPCAT 5. In the control group, two out of three participants were from more affluent DEPCAT 1-4, with one participant in DEPCAT 6.

Table 3.46 Demographic Descriptors of 6 Month Quitters

Log	Allocation	Hygienist	Sex	DEPCAT	Age
1	I	Blue	F	3	53
2	I	Green	F	4	28
39	I	Red	F	3	33
60	I	Green	F	4	37
83	I	Green	F	1	35
103	I	Blue	F	5	38
21	C	Red	F	6	32
43	C	Red	F	4	54
118	C	Blue	F	1	49

With respect to tobacco exposure at baseline as measured by cigarettes per day, in the intervention group, quitters were more likely to be moderate or light smokers, with four out of six smoking 15 or less, one smoking 25 and one smoking 40 per day (Table 3.47). When looking at the intervention group's nicotine dependence as measured by the FTND, two quitters scored 4 or below indicating low dependence, and four scored 6 or above, indicating high or very high dependence.

With regards to the three control group quitters, the numbers of cigarettes smoked per day at baseline were 18, 20 and 30. This resulted in heterogeneity amongst their nicotine categorisation as measured by FTND, with one participant each of low, medium and high dependence.

**Table 3.47 Smoking History, Physiological Dependency & Intention to Quit
at Baseline of 6 Month Quitters**

Log	Allocation	Cigs per day	Years Smoked	Pack-Years	FTND	Motivation to Quit	Stage of Change
1	I	40	37	74	8	8	3
2	I	15	10	7.5	6	8	2
39	I	10	16	8	0	7	2
60	I	25	17	21	6	8	3
83	I	15	20	15	6	8	3
103	I	10	22	11	4	6	3
21	C	30	18	27	7	5	1
43	C	20	38	38	4	6	2
118	C	18	33	30	5	7	3

Concerning years smoked, in the intervention group, five out of six had smoked previously for between 10 and 22 years, with one smoking for 37 years. With respect to pack-years, five out of six had baseline levels between 7.5 and 21 pack-years, with one participant having an exposure of 74 pack-years.

The control group quitters had a higher baseline smoking exposure than those from the intervention group, with the former participants having smoked for 18, 30 and 33 years, which translates into 27, 30 and 38 pack-years.

With regards to 'Stage of Change' at baseline, four out of the six intervention group quitters were category 3 (want to stop) with four also scoring 8 on the Motivation Scale at baseline. There was more heterogeneity amongst the control group, with one in each stage and the three scores on the Motivation Scale being 5, 6 and 7.

3.6.3.6 Self-Reported Pharmacological Use in Quitters at 6 Months

Table 3.48 shows reported use of pharmacological support, including NRT and Zyban, by those participants biochemically validated as quitters at 6 months.

Table 3.48 Use of Nicotine Replacement Therapy by Quitters (6 Months)

Log	Allocation	Hygienist	NRT or Zyban use
1	I	Blue	Patches(Nic)
2	I	Green	Patches(Nic)
39	I	Red	Patches(Nic)
60	I	Green	Patches(Nic)
83	I	Green	Patches(Nic)
103	I	Blue	Patches(Nic)
21	C	Red	Zyban
43	C	Red	Patches(N/elle)
118	C	Blue	Patches(NQ)

Nic= Nicorette (brand of NRT in patches or gum form, provided free in trial)

N/elle = Nicotinelle

NQ = Niquitin

All reported using some form of pharmacological support in quitting. Eight of the nine quitters used patches of some kind and one participant used Zyban. All intervention quitters reported using Nicorette patches which were given free of charge by the hygienists working on the trial. Of the patients in the control group, one reported Zyban use, one reported use of Nicotinelle patches and one reported use of Niquitin patches.

One participant (83) had changed their method of nicotine replacement therapy: at the 3-month mark this individual reported using lozenges (Niquitin), whereas at the 6-month point, Nicorette patches were being used.

3.6.3.7 Trial Participants who Relapsed Back to Smoking

Table 3.49 summarises the data obtained from the six participants who self-reported and were biochemically validated as having quit at 3 months, and who reported relapsing at 6 months. Most subjects who reported smoking again had cotinine levels above the cut-off point. None of the subjects reported NRT use. One subject had a low level of cotinine (around 20ng/ml) with a CO value of 9ppm, both borderline values in assessing smoking status. Another had low cotinine, 21ng/ml, with a higher CO of 13. Information was also collected on the participants' number of cigarettes, and a number report smoking at low levels (below 10 per day).

Table 3.49 Relapsers at 6 Months (Participants who at 3 months had quit, and now report smoking again)

Log	Allocation	Hygienist	Self report	COT (ng/ml)	CO (ppm)	NRT Use at time of sampling
36	I	Red	S	95	6	no
81	I	Blue	S	143	19	no
82	C	Blue	S	170	3	no
86	I	Blue	S	20	9	no
50	I	Red	S	74	3	no
113	I	Blue	S	21	13	no

3.6.4 Secondary Outcomes at 6 Months

Those participants who classified themselves as smokers six months after recruitment, were asked a number of questions about possible changes in their smoking behaviour. Questions covered included details about attempts at quitting, as well as reduction in smoking and changing to a low tar brand.

3.6.4.1 Self-Reported Attempts at Quitting

When looking at quit attempts between 3 and 6 months, Table 3.50 shows that 83% of the intervention group reported at least one attempt, compared to 56% of the control group. This result was of statistical significance. Forty three percent of the intervention participants and 28% of the control group reported two or more quit attempts. The difference was not statistically significant.

With regard to the duration of quit attempt, 60% and 47% of the intervention and controls respectively had abstained for 24 hours or more. This difference was not statistically significant. However, when asking participants about a longer and more sustained quit attempt of one week or more, a significant difference was seen, with 47% and 16% of the intervention and control groups respectively, reporting a quit attempt of this duration.

Table 3.50 Self Reported Quit Attempts - Number and Duration at 6 Months

Quit attempts:	Number (%) of Participants Reporting Quit Attempts				
	All n=62	Intervention n=30	Control n=32	p-value	95% CI (I-C)
In last 3 months	43 (69%)	25 (83%)	18 (56%)	0.033	(3, 53)%
2 or more	22 (35%)	13 (43%)	9 (28%)	0.260	(-11, 41)%
24 hours or more	33 (53%)	18 (60%)	15 (47%)	0.330	(-13, 40)%
1 week or more	19 (31%)	14 (47%)	5 (16%)	0.018	(6, 56)%

3.6.4.2 Changes in Smoking Behaviour

Table 3.51 indicates that a high number of intervention (93%) and control (81%) participants delayed smoking for greater than 5 minutes. A relatively small number of participants reported inhaling less (23% of the intervention group and 16% of the control group). With regard to smoking less of a cigarette, 47% of the intervention

group took this action, compared to 41% of the control group. When asked about brand changing and using a low tar cigarette, 40% of the intervention group self-reported taking this action, compared to 28% of the control group.

There were no statistically significant differences with respect to any of the above changes in smoking behaviour. The 95% confidence intervals are wide, and there is some evidence of the intervention group faring better than control.

With respect to asking participants whether they reduced their number of cigarettes, 67% of the intervention group reported they had reduced their intake, compared to 56% of the control group. This difference was not statistically significant.

Table 3.51 Changes in Smoking Behaviour for Participants at 6 Months

	Number (%) of Participants				
	All n=61	Intervention n=30	Control n=32	p-value	95% CI (I-C)
Delay Smoking for >5 min	54 (87%)	28 (93%)	26 (81%)	0.380	(-10, 38)%
Inhale Less of a Cigarette	12 (19%)	7 (23%)	5 (16%)	0.546	(-17, 35)%
Smoke Less of a Cigarette	27 (44%)	14 (47%)	13 (41%)	0.688	(-20, 34)%
Changed to Low Tar Cigarettes	21 (34%)	12 (40%)	9 (28%)	0.386	(-14, 38)%
Reduced Number of Cigarettes per Day	38 (61%)	20 (67%)	18 (56%)	0.430	(-14, 38)%

However, the median self-reported percentage reduction in cigarette intake was 45% for the intervention group and 22.5% for the control group. This was statistically significant (Table 3.52).

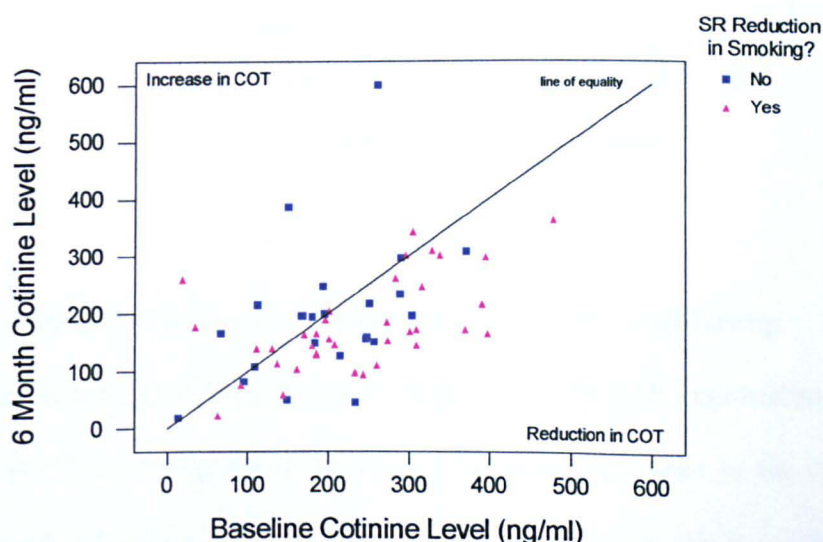
Table 3.52 Percentage Reduction in Cigarette Intake for Participants at 6 Months

	All n=50	Intervention n=26	Control n=24	p-value	95% CI (I-C)
Median	27.0	45.0	22.5	0.005	(4, 33)%
IQ Range	0.0-50.0	18.8-61.5	0.0-32.0		
Range	0-90	0-90	0-50		

3.6.4.3 Relationship of Self-Reported Smoking Reduction in Cigarettes and Cotinine Levels at Baseline and 6 Months for Individual Participants

Figure 3.12 shows levels of cotinine at baseline and at 6 months, plotted for those who did and did not report having reduced smoking. As was previously seen at the 3-month time point, not all of those who reported reducing smoking showed a concomitant reduction in cotinine levels.

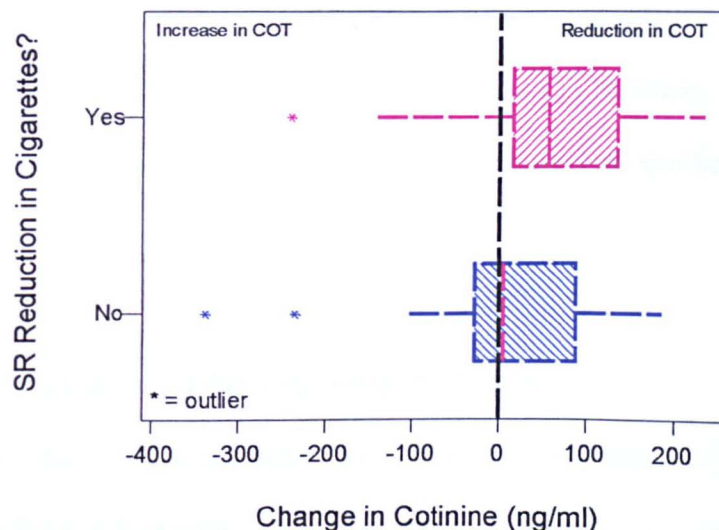
Figure 3.12 Relationship of Self-Reported Reduction in Cigarettes and Cotinine Levels for Individual Participants at Baseline and 6 Months



3.6.4.4 Relationship of Change in Cotinine Levels between Baseline and 6 Months and Self-Reported Reduction in Cigarettes

Figure 3.13 illustrates the average reduction in cotinine levels for those who reported reducing smoking (coded in blue) and those who did not (coded in pink). A significantly higher mean reduction, 61 (SD 90)ng/ml, was seen in the group who reported reducing their number of cigarettes smoked, compared to the group who did not report reducing their smoking (2 (SD 114)ng/ml); ($p=0.040$, 95% CI (I-C)=(3,114)ng/ml).

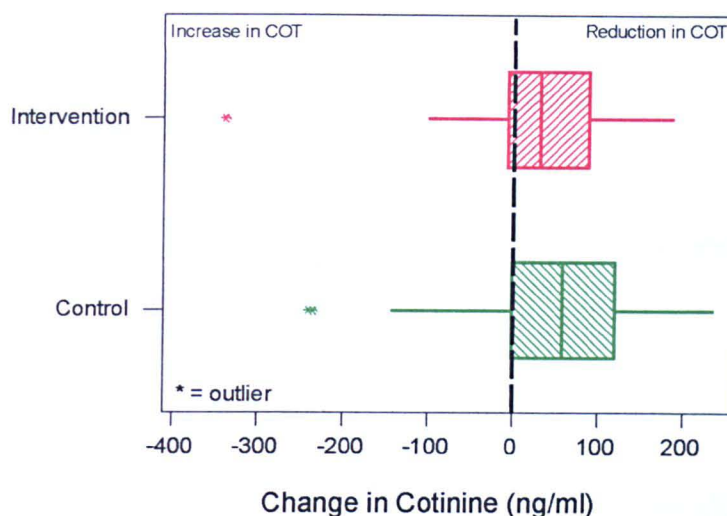
Figure 3.13 Boxplot of Cotinine Levels and Self-Reported Reduction in Cigarettes at 6 Months



3.6.4.5 Six Month Reduction in Cotinine Levels by Allocated Group

When looking at the mean reduction in cotinine levels for both intervention and control groups (Figure 3.14), a slightly higher mean reduction was seen in the control group (coded in green: 48 (SD 111)ng/ml), than in the intervention group (coded in red: 28 (SD 95)ng/ml). There was no statistically significant difference between intervention and control groups ($p=0.454$, 95% CI (C-I)=(-33,72)ng/ml).

Figure 3.14 Boxplot of Change in Cotinine Levels by Allocated Group at 6 Months



3.6.5 Changes of Intention to Stop and Stay Stopped at 6 Months

All participants, i.e. quitters and non-quitters, were asked at baseline, 3 and 6 months about whether they considered themselves to be 'contented smokers', 'concerned smokers' or 'wanting to stop'.

3.6.5.1 'Stage of Change'- All Participants at 6 Months

Table 3.53 details the baseline measurements of all trial participants and the 'stages' these participants held at 6-months. In addition to the categories of 'contented smoker', 'concerned smoker' (want to quit in the next 6 months) 'want to stop' and 'quitter', additional categories are shown relating to 'maintainers' (those smokers who were quitters at both 3 and 6 months) and 'relapsers' (those smokers who were quitters at 3 months but had returned to smoking by 6 months).

Those participants who made positive behaviour change and moved forward in the 'Cycle of Change' are coded in pink. Those participants for whom there was no change between baseline and six months are coded in blue. Some participants moved

backwards in the cycle and reported being less likely to quit and these are coded in green.

Table 3.53 Shift in ‘Stage of Change’ for All Participants between Baseline and 6 Months

Status at Baseline	Status at 6 months					
	Contented	Concerned	Want to Stop	Quitter	Maintenance	Relapse
Contented	5	4	-	-	1	
Concerned		19	7	1	2	2
Want to Stop			6	1	4	4

As can be seen from Table 3.53 for all trial participants, 20 individuals moved forwards in the ‘Cycle of Change’ (coded in pink), either by reporting being more likely to quit, or quitting and maintaining their quit attempt. With regards to moving backwards in the ‘Cycle of Change’ (coded in green), there were 21 individuals who either reported being less likely to quit or relapsed. Thirty individuals made no change between baseline and 6 months.

3.6.5.2 Shift in ‘Stage of Change’ for Intervention Group at 6 Months

Table 3.54 shows changes in position of the ‘Cycle of Change’ for those participants in the intervention group. There were 13 participants who moved forward (coded in pink) and either reported being more likely to quit, or quit and maintained their quit attempt. Twelve individuals moved backwards in the ‘Cycle of Change’, either by reporting being less ready to quit at 6 months, than at baseline or by relapsing. With respect to making no changes between baseline and 6 months, there were 11 individuals in this category (coded in blue).

Table 3.54 Shift in ‘Stage of Change’ for Intervention Group at 6 Months

Status at Baseline	Status at 6 months					
	Contented	Concerned	Want to Stop	Quitter (action)	Maintenance	Relapse
Contented	1	3	-	-	-	0
Concerned	3	7	4	1	1	1
Want to Stop	0	5	3	1	3	3

3.6.5.3 Shift in ‘Stage of Change’ for Control Group at 6 Months

Table 3.55 shows the changes for the control group. Seven individuals reported moving forwards in the cycle, nine moved backwards and 19 participants made no change.

Table 3.55 Shift in ‘Stage of Change’ for Control Group at 6 Months

Status at Baseline	Status at 6 months					
	Contented	Concerned	Want to Stop	Quitter (action)	Maintenance	Relapse
Contented	4	1	-	-	1	
Concerned	0	12	3	-	1	1
Want to Stop	1	6	3	-	1	1

3.6.6 Number of Treatment Visits for Quitters and Non-Quitters at 6 Months

The median number of visits for quitters at 6 months was 7 (range 6-8), while the median number of visits for trial participants categorised as smokers at 6 months was 6 (range 1-8).

3.7 One Year Outcomes

Trial participants were followed-up at the one-year mark, by telephone interviews in the first instance. If contact was unsuccessful, a short postal questionnaire was sent to their home address.

If the individual claimed to have stopped smoking, a request was sent out by post for a sample of the patient's saliva for cotinine analysis.

3.7.1 Follow-up of Participants at all Time Periods

Table 3.56 details the number of participants followed up at the different time periods.

Table 3.56 Comparison of Follow-up of Participants at all Time Periods

	Intervention	Control	Total
At baseline	59 (51%)	57 (49%)	116 (100%)
At 3 months	52 (88%)	50 (88%)	102 (88%)
At 6 months	36 (61%)	35 (61%)	71 (61%)
At 1 year	33 (56%)	23 (40%)	56 (48%)

As the time period increased from baseline, the response rate diminished. At the one year point, contact was established with 56 (48%) of the original trial participants. At this time, information was collected from more individuals in the intervention group (56%) than in the control group (40%).

3.7.2 Details of Patient Contacts

Information on the type of contact established and any barriers to follow-up, are detailed in Table 3.57.

Table 3.57 Follow-ups of Participants at 1 Year

Telephone contact with patient	36 (31%)
Postal contact established with patient	20 (18%)
Patient details incorrect	10 (8%)
Patient wants no contact	7 (6%)
No contact established	42 (36%)

Telephone contact was established with 36 of the original trial participants, and postal contact was made with a further 20 individuals. Incorrect patient details and patients wanting no further contact accounted for a further 17 individuals. Attempts were made to obtain postal information from the remaining 42 trial participants, and no information was returned from the individuals concerned.

3.7.3 Primary Outcomes at One Year

Participants were asked whether they considered themselves to be smokers or not. In Table 3.58, the results of the self-reported quitters are displayed.

Table 3.58 Participants' Self Reported Smoking at 1 Year

Are you a smoker?	Intervention	Control	All
No	7 (21%)	3 (13%)	10 (18%)
Yes	26 (79%)	20 (87%)	46 (82%)
Total	33	23	56

The self-reported seven and three quitters represented quit rates of 12% and 5% of the intervention and control patients recruited respectively. However, the difference between intervention and control in terms of the proportion of participants reporting as having quit did not reach statistical significance ($p=0.411$, 95% CI (I-C)=(-7, 25)%).

As discussed there was no collection of CO values, but those respondents who claimed to have quit were asked for postal cotinine. The results of this can be seen in Table 3.59.

Table 3.59 One Year Summary Table of Biochemical Measure (COT) and Use of NRT at time of sampling for Self-Reported Quitters

Log	Allocation	Hygienist	Self report	COT (ng/ml)	NRT Use at time of sampling
1	I	Blue	NS	<2	no
13	I	Green	NS	<2	no
15	I	Blue	NS	none	no
38	I	Green	NS	373	no
39	I	Red	NS	<2	no
52	I	Green	NS	<2	no
103	I	Blue	NS	none	no
20	C	Green	NS	385	no
21	C	Red	NS	<2	no
43	C	Red	NS	<2	no

Trial participants 1, 103, 21 and 43 were quitters at 3 and 6 months also, with participant 39 being a quitter by 6 months. Participant 38 was a 'recent' quitter, i.e. within the last 6 months. Patients who did not provide samples for biochemical verification were deemed to be smoking again.

Cotinine salivary samples were received from eight out of the ten self-reported quitters. Cotinine measurements confirmed that six of these individuals were non-smokers (Table 3.59). Participant 20 during the telephone interview described themselves as a quitter, but by the time the postal cotinine had arrived, this individual was smoking again. Participant 38 would appear to be a 'deceiver'. None of the trial participants reported on NRT use at the one-year time point.

Table 3.60 Definitive Quitters as measured by Self-Report and Cotinine at 1 Year

Log Number	Allocated Group	Self Report	Cotinine	Category
1	I	✓	✓	quitter
13	I	✓	✓	quitter
39	I	✓	✓	quitter
52	I	✓	✓	quitter
21	C	✓	✓	quitter
43	C	✓	✓	quitter

Blue=Intervention Purple= Control

In summary, on the basis of biochemical verification, data were available for 8 individuals, which confirmed 4 intervention and 2 control participants to have quit smoking (Table 3.60).

Therefore, of the patients followed-up, this results in a quit rate of 12.1%, compared to 8.7% in the control group. The difference between intervention and control groups was not statistically significant ($p=0.798$, 95%CI (I-C)=(-21.0, 32.0)%).

Of the patients recruited at baseline, the four and two definitive quitters represented quit rates of 6.8% and 3.5% of the intervention and control patients recruited respectively. However, the difference between intervention and control groups, in terms of the proportion of participants defined as having quit, did not reach statistical significance ($p=0.669$, 95% CI (I-C)=(-9.0, 21.5)%).

3.7.4 Information from Smokers

Participants were asked, if they smoked, whether they considered themselves to be occasional or regular smokers. All 46 smokers who replied consider themselves to be regular smokers. When asked if they had tried any further quit attempts or felt more able to try again, 24 smokers (15 intervention and 9 control) replied in the affirmative. When asked about why they smoked at least as much as they did a year ago a number of explanations were given. The results are listed in Table 3.61.

Table 3.61 Reasons for Not Quitting by Participants Still Smoking at 1 Year

Wasn't ready to give up	2
Related to stress	9
Patches didn't work	0
Too hard to give up	12
Changed my mind	0
Individual problems /circumstances	21
• habit	11
• enjoyment	3
• boredom	2
• addiction	1
• lack of willpower	1
• don't want to	1
• stressful domestic situation	1
• routine	1

Number of responses = 44

Chapter 4 Discussion

4.1 Introduction

The discussion of the body of work concerning the use of cotinine is to be found in Chapter 2. In this chapter, the main findings relating to the smoking cessation trial detailed in Chapter 3 are discussed.

In the initial section below, the theme of smoking cessation has been placed in the overall context of tobacco control measures. In the second section, methodological issues relating to the trial design are discussed. The findings of the study are then examined and compared with previous work. In the last sections, the implications of this body of work, including its limitations will be discussed.

4.2 Background

As previously mentioned, smoking cessation is but one small part, albeit an important one, of the whole tobacco control agenda. Other measures include reducing the demand for tobacco products through prevention, and addressing the issues of environmental tobacco smoke, through enabling the legislative and public health agenda. Comprehensive bans and restrictions on advertising, together with legislation relating to the packaging and labelling of cigarettes, are also important in controlling tobacco use (Jamrozik, 2004). Currently in Scotland, the focus is very much on environmental smoke issues, with the Scottish Parliament currently consulting on a widespread, or more restricted, smoking ban in public places (Scottish Executive, 2004b).

Smoking cessation is, however, still seen as an important area within this overall agenda and, in Scotland, there is to be increased funding and expansion of such services (Scottish Executive, 2004a).

Smoking cessation and its delivery is a complex issue. With the rise in the number of specialist smoking cessation services in both England and Scotland, this presents a number of service delivery possibilities with respect to smoking cessation. Issues relating to the role of dental team members, and the various options of how matters can be taken forward, are discussed in Section 4.5.

4.3 Methodological Issues

4.3.1 Design of Trial and Sample Size calculation

There has been limited research in the UK regarding smoking cessation in the dental setting, especially utilising a randomised controlled trial design (RCT). This was the methodology of choice for the study reported here. Typically, RCTs seek to measure and compare different events that are present or absent after the participants receive the interventions (Jadad, 1998).

Usually, one of the interventions is regarded as a standard of comparison or control. The control can be conventional practice, a placebo, or no intervention at all. In the case of this trial, all participants received at their first visit both verbal information about the role smoking plays in periodontal disease, and ‘very brief advice’ to quit from the consultants as part of standard clinical care. In addition, all patients registered on the trial received an information sheet. Therefore, the control group were subject to some advice, albeit ‘very brief’, from the consultants at their first appointment. In summary,

the intervention group received advice and help in the form of the 5As and the offer of free NRT, whereas the control group received 'usual care', as detailed above.

With regards to the other previously reported dental smoking cessation studies, in the Macgregor trial (1996) participants were systematically allocated to either the intervention or control group (i.e. using alternate allocation). The trial of Smith *et al.* (1998) did not use an RCT design and all participants were given the same intervention. The largest RCT of dental hygienists and smoking cessation was by Severson *et al.* (1998) in which, after stratification by size of practice (as defined by number of hygiene visits/week) and number of years the dentist was in practice, the dental practices were then randomly allocated to one of three groups, 'usual care', 'minimal' or 'extended' intervention. The trial of Cohen *et al.* (1989) randomly allocated private dental practices to one of four groups 'control', 'reminder', 'gum' or 'reminder and gum'.

There was no uniformity in the studies outlined above, with regard to the definition of control group. In the trial by Severson and co-workers (1998), the control leg meant 'usual care', where dentists and hygienists were free to use their clinical judgement, and some of the patients may have received some smoking information. In contrast, in the trial by Macgregor (1996), the participants in the control phase received no smoking cessation advice at all.

With respect to sample size calculation, this was based on secondary outcomes as outlined in Chapter 3. In terms of the primary outcome, to detect, for example, a 10% difference between groups with 80% power, would have required the follow-up of at least 160 patients in each group. Audit figures for the Periodontology Department in

2000 suggested that there would have been approximately 275 suitable patients per year. Therefore to recruit approximately 350 patients, would have required a recruitment period of at least 30 months, which was not considered feasible within the time constraints of this PhD. Therefore, the sample size calculation was based on the secondary outcome of reduction in number of cigarettes. Again, assuming that half of the suitable patients were recruited, a recruitment period of approximately one year was envisaged. The recruitment period for this trial actually lasted 16 months.

None of the other reported smoking cessation trials within the dental setting reported sample size calculations.

4.3.2 Choice of Intervention – 5As

The 5As approach to smoking cessation was selected as the intervention of choice for a number of reasons. Firstly, when this trial was planned in 2000/2001, the methodology recommended for delivering smoking cessation advice in primary care in Scotland was the 5As (Health Education Board for Scotland and ASH Scotland, 2001). This guidance had, in turn, been influenced by the American Guidelines for health professionals (Fiore *et al.*, 2000). This latter body of work was subsequently reflected in the approach adopted in the delivery of smoking cessation in a number of settings in the USA and Australia (Litt, 2002; Solberg *et al.*, 2002). There is also recent evidence of the 5As being used with patients in various settings, including primary and secondary care (Litt, 2002; Solberg *et al.*, 2002) and with several groups, including pregnant women and asthmatic patients. In addition, the only smoking cessation trial in the UK in general dental practice had used a precursor approach, known as the 4As (Smith *et al.*, 1998).

An advantage of the 5As approach to the delivery of smoking cessation advice is that there is a structure to the methodology which makes it relatively easy to teach to health professionals, such as dentists and hygienists, for whom it is now recognised that smoking cessation is one of their responsibilities, in addition to their standard clinical care.

Other methodologies are available for delivering smoking cessation advice, such as motivational interviewing or the use of a 'stage-matched' intervention such as 'Pro-change' (University of Rhode Island, 1997). In this latter programme, information is given to the trial participant depending on an assessment of the individual's 'Stage of Change'. This programme has been designed for use in primary care, and has proved very popular for use in UK pharmacies (Anderson and Mair, 2000).

Both of the above methodologies were briefly considered, but discounted for use in this trial. The motivational interviewing was thought to be too time-consuming to undertake in this setting, and the 'Pro-change' programme was considered to be untried for use by dental staff.

Therefore, the 5As was selected as the most appropriate methodology, for use by dental hygienists in this particular setting, for reasons relating to time and ease of use.

4.3.3 Choice of Baseline Data Collection

4.3.3.1 Choice of Biographical Data

Patient data collected included age, occupation and postcode (to enable categorisation of DEPCAT). As the sample was overwhelmingly female (71%) and the patients' description of their job title did not easily translate into a category for use by the Registrar General's Classification, it was decided to use the Carstairs DEPCAT Index as the reported socio-economic indicator. A DEPCAT Score was obtained for all patients from postcode sector data. Patients' telephone numbers and addresses were also recorded to allow follow-up contacts to be made.

4.3.3.2 Choice of Nicotine Dependence Measures

In attempting to determine a patient's nicotine dependence, three composite measures were collected; *Heaviness of Smoking Index* (2 questions), *Fagerstrom Test for Nicotine Dependence* (6 questions) and *Fagerstrom Tolerance Questionnaire* (8 questions).

The most commonly used index is the FTND, and the briefest one the *Heaviness of Smoking Index* (Heatherton *et al.*, 1991). With respect to the Fagerstrom Tolerance Questionnaire, the present study found there was little advantage obtained from asking the two additional questions concerning the brand and type of cigarette, and level of inhalation. Although patients were able to detail their brand of cigarette, often insufficient information was given to allow determination of the level of nicotine of their chosen cigarette. In addition, as all participants recruited at baseline inhaled smoke, there was very little variation accounted for by this question.

The indices of choice with regards to research and evaluation of smoking cessation programmes would appear to be the *Heaviness of Smoking Index* for brevity, and the *FTND* for more detailed information (Heatherton *et al.*, 1991). In Scotland, the specialist smoking cessation services are presently collecting information based on the *Heaviness of Smoking Index* (PATH, 2003).

4.3.3.3 Choice of Motivation to Quit Measures

Two motivation to quit measures were used, the Motivation Index by Foulds (1996) and a modified form of 'Stage of Change', which was influenced by the work of Prochaska and DiClemente (1983, 1993).

While there is much uniformity amongst researchers when using the FTND (Hetherton *et al.*, 1991), there is some variation in the questionnaires used relating to the 'Stage of Change', particularly when categorising trial participants to the various stages. Additionally, researchers sometimes use different terms for the same stages, for example, 'precontemplators' can be known as 'not interested in quitting', 'contemplators' can be known as 'interested in quitting (within the next 6 months)', and those in the 'preparation' stage can be known as 'want to stop (within the next month)'.

In addition to the differing terminology, the definition of the stages can vary, particularly with the 'preparation' stage. A number of researchers define those individuals as being in the 'preparation' stage if they want to quit within one month and have had a quit attempt in the last year (Prochaska and DiClemente, 1983; Prochaska and Velicer, 1997; Etter *et al.*, 2003). Others, however, define the 'preparation' stage solely as wanting to quit within the next month (Foulds, 1996; Butler *et al.*, 1999;

Hughes *et al.*, 2000; Etter and Perneger, 2001). This latter interpretation is the version that was used in this trial. Utilising only the timeframe for intention to quit enables a more standardised approach to be taken when categorising intention to quit at 3 and 6 months, therefore enabling movement in the 'Stage of Change' to be monitored.

Other researchers have changed the timeframe associated with the definitions of 'contemplator' and 'preparation' stages. Rohren and co-workers (1994) shortened the timeframe for classification of 'contemplator' from 6 months to one month, and produced their own definition of the various stages. Donovan *et al.* (1998) changed the timeframe for 'preparation' to a fortnight, rather than a month. Thus, when making comparisons between different studies involving 'Stage of Change', the degree of variation that may exist between the measures used has to be borne in mind.

4.3.3.4 Choice of Nicotine Exposure Measurements

With respect to lifetime exposure to nicotine, patients were asked how many years that they had smoked, and together with the information obtained relating to the number of cigarettes per day, lifetime exposure in the form of pack-years was calculated.

Pack-years, in addition to other questionnaire-derived data, can be subject to bias due to the nature of its collection, i.e. self-report (Scott *et al.*, 2001). Additionally, the pack-years measure gives an estimate of lifetime exposure based on current tobacco use and does not take into account the fact that individuals may have varied their smoking behaviour over time. However, pack-years is the only measure that is currently used as an indicator of lifetime exposure, and as such, is used in respiratory (Patel *et al.*, 2004) coronary (Chambless *et al.*, 2003) and periodontal research (Chen *et al.*, 2001).

4.3.3.5 Use of Biochemical Monitoring including Cotinine and Carbon Monoxide

It was decided to use both carbon monoxide and cotinine as a means of biochemical validation. It is known that cotinine measurement is more accurate with respect to detecting exposure to tobacco smoke over a longer time frame than carbon monoxide (SRNT Subcommittee on Biochemical Verification, 2002). In relation to this former indicator, previous work (as detailed in Chapter 2) had refined the method of sample collection and validated the analysis using the EIA kits, as there had been very little previous research carried out in the UK using this cotinine assay. Smith *et al.* (1998) did use salivary cotinine samples for validating the tobacco exposure of the dental patients recruited to their trial, but the method of analysis was gas chromatography.

In Chapter 2, differentiation between smokers and non-smokers was straightforward, with patients being recruited either as a smoker and non-smoker, and cotinine being used to determine their daily exposure to nicotine. When cotinine is being used with smokers as a means of biochemical verification, particularly during or after a quit attempt, the picture was more complex. It was part of the recruitment criteria, that participants had to smoke at least 10 a day, and all recruits reported at least this exposure. At 3 months, it was in some cases difficult to categorise individuals into quitters or non-quitters, firstly due to some participants being ‘light smokers’ and secondly due to the use of NRT at this time point.

With respect to the CO monitoring, two carbon monoxide monitors were lent to the project, free-of-charge by *Smoking Concerns* (NHS Greater Glasgow). CO readings were taken at every visit for participants in the intervention group, as a motivational

tool, to encourage those smokers who had not quit, as well as a means of reinforcement for those individuals in the process of quitting.

In addition, CO was also measured at the time points used for cotinine sampling. This enabled a comparison of the two measures of determining smoking exposure, and the preliminary findings of this accessory body of work was the subject of a research abstract and is included in Appendix 13. As this strand of research was not included in Chapter 3, which focuses on the efficacy of the smoking cessation trial with respect to primary and secondary outcomes, it will not be discussed further.

Most of smoking cessation work, including the national evaluations of specialist smoking cessation services, is validated by the use of CO, rather than cotinine, because of resource implications. Additionally, CO being non-nicotinic, is of use in validating smoking cessation in the presence of NRT, and was used in this way, within this trial.

Some researchers dismiss the use of biochemical monitoring, and rely purely on self-report (Sinclair *et al.*, 1998; Butler *et al.*, 1999). The reasoning behind this is that they feel the ‘deceivers’ obtained using this methodology are few in number and the economic costs, particularly in relation to staff time, do not justify its use.

However, it can be argued that use of biochemical validation provides a more complete picture, and it is firmly recommended in the position paper by the Society for Research on Nicotine and Tobacco (SRNT Subcommittee on Biochemical Verification, 2002). As detailed in Chapter 2, the half-life of cotinine is around 20 hours, and can detect an individual who has smoked within the past week. Therefore there is a recommendation

that a period of seven days is used to assess compliance with non-smoking in most studies, and to ensure that there are no false positives (SRNT Subcommittee on Biochemical Verification, 2002).

It could be postulated that the explicit use of biochemical monitoring helps reduce the number who attempt to give false information. In this project, one 'deceiver' was detected at three months. Additionally, at one year, two individuals were identified who described themselves as non-smokers, but cotinine levels verified that this was not the case. The Smith trial also detected two deceivers (Smith *et al.*, 1998).

One study where there was a noticeable difference between self-report and biochemically validated status was the *Scottish Health Survey* in 1998 (Shaw *et al.*, 2000). According to the information sheet issued to trial participants, these individuals did not know that their salivary samples were to be used to measure tobacco exposure. There was an under-reporting of prevalence of smoking, especially by males, and this was most marked in the younger age-group (9% under-reporting in the 16-24 year age group).

Additionally, Velicer *et al.*, (1992) reported that in medical settings, such as those involving patients with heart disease or pregnant women, the difference between self-reported quitting and biochemical verification of quitting could be as high as 13%.

These results clearly show the importance of biochemical validation. Therefore, to evaluate smoking cessation more accurately, it is essential that some form of biochemical validation is used. Of the two methodologies, cotinine is the validator of

choice because of its long half-life (Jarvis *et al.*, 1987). However, if patients are using NRT, CO monitoring can be useful. One newer means of biochemical verification involving cotinine is the use of the near-patient test (Cope *et al.*, 2000). Further work using this technique is required to fully develop its potential.

4.3.3.6 Choice of Measures of Abstinence in Smoking Cessation Trials

There are a number of measures that can be used to determine smoking cessation rates at follow-up including point prevalence, prolonged abstinence and continuous abstinence. Several papers have discussed the uses of these measures in detail (Velicer *et al.*, 1992; Hughes *et al.*, 2002; Hughes *et al.*, 2003; Velicer and Prochaska, 2004).

In this trial, the measure of point prevalence was used, with prolonged abstinence measures also reported for 6-month outcomes.

Within the dental literature, there is little use of continuous abstinence measures, with most studies reporting point prevalence measures (Secker-Walker *et al.*, 1988; Macgregor, 1996; Smith *et al.*, 1998). One trial reported that they used sustained abstinence, with smokers reporting that they ‘had not smoked at all, not even a puff’ during the last seven days before assessment at 3 and 12 months (Severson *et al.*, 1998). This methodology is similar to the follow-ups in this present trial, with cotinine testing substituted for the question detailed above.

Hughes *et al.* (2003), in a position paper for the *Society for Research on Nicotine and Tobacco*, discuss issues relating to measures of abstinence in smoking cessation clinical trials. They describe one type of trial which they call a ‘cessation induction’ trial, an

example of which would be physicians giving advice to all smokers. In a trial of this design, smokers may not be currently trying to quit, and with respect to patient follow-up, they recommend this should be related to the initiation of the intervention, with point prevalence measures being reported at 6 and 12 months and a prolonged abstinence of ≥ 6 months duration.

The second type of trial described in this paper is an '*aid-to-cessation*' trial, an example of which would be group behaviour therapy or a medication trial. This type of trial tests a treatment among smokers currently willing to quit. In this case, the experimenter, not the subject, sets the quit date. It is suggested that, in this type of trial, follow-up of smokers willing to try stopping on the set quit date should relate follow-ups to the quit date and report 6 and 12 month abstinence rates.

In the trial described in this thesis, there are more parallels with the 'cessation induction', rather than the 'aid-to-cessation' trial. One of the main differences focuses on patients' intentions. Patients, per se, do not come in the first instance for smoking cessation treatment to the Periodontal Department at Glasgow Dental Hospital, they attend initially for periodontal treatment. Therefore, there are differences between this group, and the group of 'clients' who turn up for treatment at a specialist smoking cessation service.

4.3.3.7 Choice of Monitoring Time Points

There is debate over the timeframes used to measure 'success' in smoking cessation trials (Hughes *et al.*, 2003). A number of timeframes are available: 24 hours, 1 week, 1 month, 3 months, 6 months, and one year, or longer (2 to 3 years).

Researchers are in agreement that one-year outcomes are desirable, whether self-reported or biochemically validated (Hughes *et al.*, 2003). However, there is a direct relationship between length of follow-up and patients lost to follow-up, with a higher number lost at the one-year mark, than at the six-month time frame (Velicer *et al.*, 1992). Where there is some debate, is over what other timeframes can be used to determine efficacy. One month is the time frame used by UK specialist smoking cessation services and this often coincides with the end of a course of group treatment. Quit rates are higher at this time point compared with longer time frames, with the English Specialist Smoking Cessation Services reporting a quit rate of 57% (of those setting a quit date) abstinent at one month, self-reported (Department of Health, 2004). One month outcomes include a grace period of two weeks, in which the smoker may lapse, but require the smoker not to have smoked, even a puff, in the two weeks preceding the collection of one month data. In Scotland, one-month outcomes are to be collected, but are to be biochemically validated with CO (PATH, 2003). The Specialist Smoking Cessation Services in Scotland intend also to collect self-reported three-months outcomes.

Follow-up at three months provides a longer term view of quitting, though a number who had quit at one month will have relapsed. At six months, some participants who had quit at three months will continue to be abstinent, and some of those participants who had quit using NRT, may have stopped taking the medication. In addition, some may have relapsed. At one year, the quitters will be more akin to a non-smoker, though relapse will still be possible.

With respect to dental smoking cessation interventions, follow-ups vary: from 3 months and 12 months (Severson *et al.*, 1998), 9 months (Smith *et al.*, 1998), between 3 and 12 months (Macgregor 1996), 6 months (Secker-Walker *et al.*, 1988), 6 and 12 months (Cohen *et al.*, 1989). A contemporaneous smoking cessation trial running in Newcastle Dental School in the Periodontology Department used similar time frames to this project, i.e. 3 and 6 months and one year (Heasman *et al.*, 2004).

Given unlimited resources, there could be an argument for taking measurements at 1, 3, 6, and 12 months. However, this would require a great deal of staff input, as patient follow-ups can be time-consuming and frustrating, and the possibility would arise that the process of obtaining outcome data could consume more resources than was required to deliver the intervention in the first place. There would also be a considerable and unsustainable commitment required from the patients for multiple assessments. Most interventions, be they service-orientated or research, often do not have the luxury of multiple follow-ups, and therefore decisions have to be made about what timeframes to use, to give maximum comparability with work already completed.

4.3.3.8 Reporting of Patient Follow-ups

With regard to success rates, there are two ways in which the data can be presented. Success rates can be calculated for those from whom data were collected at a particular time point, and a number of researchers use this methodology (Secker-Walker *et al.*, 1988; Macgregor, 1996, Butler *et al.*, 1999). Others estimate success rates with all participants lost to follow-up being deemed to be smokers (Smith *et al.*, 1998; Silagy and Stead, 2004; Rice and Stead, 2004). One study reports both (Cohen *et al.*, 1989), and one bases outcomes on patients followed-up for secondary outcomes, but calculates

success of quitting at 3 and 12 months using all patients registered to the trial, assuming all patients lost to follow-up are still smokers (Severson *et al.*, 1998). Within this trial, it was decided to report both outcomes, to enable comparison with work already carried out in the dental smoking cessation field.

4.3.4 Choice of Pharmacological Support

With regard to the provision of pharmaceutical support for the trial, it was decided, in association with advice from *Smoking Concerns* (NHS Greater Glasgow), to use only nicotine patches and gum, and not include other forms of NRT such as lozenges and inhalers. This was considered most practical from a stock control perspective. Access to NRT is now considered standard practice for patients in smoking cessation trials (Silagy *et al.*, 2004).

The use of Zyban was discussed and discounted, as at the time this trial was being planned, there was some controversy over the use of Zyban. In addition, the funding and prescribing mechanisms for delivering this drug to the patients would have been complex, and would have required referral back to the general medical practitioner.

4.3.5 Primary Outcomes

As discussed previously, it was decided to report outcomes at 3 and 6 months and one year. The three smoking cessation outcome measures used were self-report, and the two biochemical measures of salivary cotinine measurement and CO levels in an exhaled air sample. Measurement of follow-up was in association with the patient's registration date into the study and not with the patient's quit date. Other dental and medical studies

have used this methodology (Secker-Walker *et al.*, 1988; Severson *et al.*, 1998; Smith *et al.*, 1998; Butler *et al.*, 1999).

The main measure used was point prevalence, biochemically validated by salivary cotinine, which confirms the absence of nicotine over the previous seven days. In the presence of NRT, smoking cessation was validated by the use of CO, and this is in line with the recommendations of Hughes *et al.* (2003). The other measure used was that of prolonged abstinence. This was reported for 6-month outcomes for this current study.

4.3.6 Secondary Outcomes

The secondary outcomes used within this study were reported quit attempts of varying duration and reduction in smoking, for example, by lowering the daily number of cigarettes smoked.

Researchers differ in their opinions as to whether there is merit in looking at secondary outcomes in smoking cessation programmes. One school of thought is that smokers have to 'prepare' to quit and that making changes to smoking behaviour such as short-term quit attempts, or cutting the number of cigarettes, should help to increase the smokers self-efficacy and make them more ready to quit (Hughes, 2000; Carpenter *et al.*, 2003). However, others feel that giving smokers the soft option is a delaying tactic, rather than helping them tackle the ultimate goal of full cessation (Fiore *et al.*, 2000).

4.4 Discussion of Results

4.4.1 Introduction

The amount of literature available in the smoking cessation field in both primary and secondary care is vast, especially with respect to particular target groups such as pregnant women, adolescents, patients with a pre-existing condition such as asthma, COPD (chronic obstructive pulmonary disease) and heart disease. Many of these groups are not directly comparable with the group under study in this thesis. Thus, the results of the present study have been discussed mainly in relation to the dental literature in this field. The one exception to this is to compare findings with those of the trial by Butler and co-workers (1999), which was set in a general medical practice, and utilised two methodologies, one 'very brief' advice and a more intensive intervention using motivational interviewing. Aspects of its data collection, especially with respect to secondary outcomes and 'Stage of Change', influenced the development of the present body of work. The trial by Butler and co-workers has been included in two recent reviews of the use of 'Stage of Change' and in both was highly rated (Riemsma *et al.*, 2003; van Sluijs *et al.*, 2004).

4.4.2 Number of Patients Recruited

There were 118 patients, 59 intervention and 59 control subjects, recruited to the trial over a 16-month period. It had been hoped to follow-up 120 patients at 3 months, but numbers fell short of this figure. A number of factors contributed to this. A previous audit carried out in the Periodontology Department, monitoring throughput of patients who smoked, gave higher numbers than the throughput of patients during the recruitment period. This was in part due to the loss of one of the consultants in Periodontology a number of months into the trial, resulting in a lower number of clinics

available from which to recruit patients. In addition, this particular consultant had been the most active in recruiting patients for the study. Due to time constraints, it was not possible to lengthen further the time period of recruitment.

With regards to patients recruited, one patient subsequently withdrew consent and one patient died, and both of these had been allocated to the control group, so final analysis was carried out on 116 patients (59 intervention, 57 control). This constitutes almost balanced numbers of participants in the intervention and control groups, which is desirable for a randomised controlled trial (Jadad, 1998). Each hygienist also had almost equivalent numbers of intervention and control patients, and the case-load of smoking cessation trial participants for each hygienist reflected the number of sessions worked per week.

4.4.3 Characteristics of Patients Recruited to Smoking Cessation Trial at Baseline

4.4.3.1 Comparability of Groups with respect to Randomisation factors

As described in the methodology, the aim of the randomisation procedure was to ensure that the intervention and control groups were similar with respect to the characteristics of age, sex, DEPCAT, level of nicotine dependence and intention to quit. This was achieved, with the exception of age, where a statistically significant difference was found. It should, however, be stressed that the difference in the mean age of 3.6 years between the two groups can be considered acceptable, as often within trials, subjects are matched within an age banding of five years.

4.4.3.2 Sex and Gender Issues regarding Participants recruited to the Trial

A high proportion of the trial recruits were female, with 71% of the total being women. Other trials have exhibited a similar level of females (Secker-Walker *et al.*, 1988; Butler *et al.*, 1999), though some have been evenly balanced (Smith *et al.*, 1998), and some have had more males (57%) (Macgregor, 1996). In some trials the gender of participants has not been reported at baseline (Severson *et al.*, 1998).

With respect to the higher number of females in the present study, this reflected the patient cohort attending the Periodontal Department at Glasgow Dental Hospital for treatment, i.e. the centre used for recruitment.

In the UK, the prevalence of periodontal disease is higher in men. On average, they have greater pocket depths and more plaque (Kelly *et al.*, 2000). However, it is known that women present more readily for regular dental care, including periodontal treatment (Bullock *et al.*, 2001).

In Scotland, smoking rates in men and women are almost equivalent (Shaw *et al.*, 2000). With respect to smoking cessation, it has been suggested that women may find it more difficult to quit than men (Perkins *et al.*, 1999; Wetter *et al.*, 1999). The reasons are not well understood, but are likely to be due to a combination of biological, psychological and social factors (Mackay and Amos, 2003).

When looking at health issues, Greaves and Barr (2000) have stated that it is important to differentiate between the impact of sex (the biological differences between men and women) and gender (the social and cultural differences experienced by women and

men). Most issues to do with smoking are gender-based. Women, especially those from a low income background, can face barriers when they try to quit smoking. There are issues related to stress, self-esteem and body image, and tobacco can be seen as a means of helping with weight control (Greaves and Barr, 2000). Physiologically, when both men and women quit, it is likely that they will put on weight in the region of 6-12 lb. This weight gain can be a negative reinforcer for many females (USDHHS, 2001b).

4.4.3.3 Deprivation Category of Participants

Approximately 50% of the trial participants were recruited from the more affluent areas of the West of Scotland, i.e. DEPCATS 1-4, with the others recruited from the more economically disadvantaged DEPCATS 5-7.

This pattern does not reflect the distribution of smokers within the population. It is known that there is a direct relationship between increasing deprivation category and smoking prevalence. Once again, the recruitment setting, i.e. a hospital periodontal department, will have influenced this finding, with a higher proportion of the smokers from the more affluent areas seeking treatment for smoking-related periodontal problems. There is a similar relationship with deprivation and dental attendance, with patients from a higher socio-economic group more likely to seek regular dental attendance (Kelly *et al.*, 2000).

With respect to the dental smoking cessation literature and deprivation, previous studies have not reported this descriptor of their patients' socio-economic background (Macgregor, 1996; Severson *et al.*, 1998; Smith *et al.*, 1998). The Butler trial (1999), conducted in a general medical practice setting, reported manual/non-manual

occupation as a means of describing the patients' occupational background. The more recent research, i.e. published in the 2000's, will be more likely to report deprivation descriptors (Bauld *et al.*, 2003).

Smokers from deprived backgrounds continue to be seen as a special target group. It is known that smoking prevalence is much higher in this group, and there are issues around the individual's efficacy and low self-confidence which can be barriers to quitting. Smoking is seen as a means of coping with the stresses of living in a disadvantaged community (Stead *et al.*, 2001). Low-income smokers tend to be more heavily dependent on tobacco, and may be more sceptical about the success of NRT (Wiltshire *et al.*, 2003). Smokers from deprived areas are also less likely to try to quit and are more likely to be unsuccessful when they do try to quit (Bauld *et al.*, 2003).

As such, attempts are being made to try to develop services that are more locally sensitive to the needs of the low-income smoker in the relevant areas in Scotland. *Partnership in Action in Tobacco and Health* (PATH) has recently funded a number of projects aiming to deal with the issues of smoking and low income. One innovative idea is the use of 'Buddies', defined as former smokers who have successfully quit, and who could be used as counsellors (May and West, 2000). This use of peer counselling helps to strengthening the smoker's self-efficacy at this vulnerable time.

In summary, from a DEPCAT perspective, participants in this trial were typical of those individuals attending the dental hospital Periodontology Department, and not typical of the West of Scotland population of smokers.

4.4.3.4 Age of Participants

With respect to this trial, the mean age of the participants was 41.2 years, i.e. middle age and this is reflected by the setting and the fact that patients attending this clinic had some evidence of periodontal disease. Often participants in smoking cessation trials are middle-aged, and may exhibit some smoking-related symptoms (Secker-Walker *et al.*, 1988; Cohen *et al.*, 1989; Smith *et al.*, 1998; Butler *et al.*, 1999).

At national level, there is much focus on tackling the problem of young smokers, 20 years and under (NHS Health Scotland and ASH Scotland, 2004). Much research effort has been put into attempting to make services appropriate and accessible for this age group, as well as preventing young people from taking up this deadly habit.

However, increasing cessation rates amongst all groups of smokers is still seen as very much a priority in Scotland, with the current planned expansion of specialist smoking cessation services (Health Scotland and ASH Scotland, 2004).

4.4.3.5 Nicotine Dependence Measures

The median *Heaviness of Smoking Index* for trial participants was three, with participants scoring from zero to six. The median FTND was five, with participants scoring from zero to 10. With reference to FTND and level of addiction, a score of 0-2 is considered very low, 3-4 is low, 5 would indicate medium addiction, 6-7 is considered high, with 8-10 very high addiction. Therefore, with respect to nicotine dependence of the trial participants, the median score of five would indicate medium addiction. However, as the scores ranged from zero to 10, it would appear that

individuals exhibited a range of nicotine dependence from very low to very high addiction.

One US dental trial reported a mean FTND score of 5.5 (Cohen *et al.*, 1989). Severson and co-workers implied that they collected such data, but indicated that as there was no difference in these measures between their three study groups, the information was not reported (Severson *et al.*, 1998). With respect to the UK dental smoking cessation studies, they did not report tobacco dependence using the FTND or *Heaviness of Smoking Index*, but tended instead, to report individual components of these indices, often in the form of number of cigarettes per day (Secker-Walker *et al.*, 1989; Smith *et al.*, 1998) or smoking within the first half-hour of waking (Smith *et al.*, 1998). These findings, in relation to the present study, are reported below.

With regards to number of cigarettes smoked, the median number for trial participants was 20 (a pack a day). Only 5% of trial participants smoked 31+ per day, with 27% smoking between 21 and 30 per day. With respect to the Smith trial, 64% smoked ≥ 20 cigarettes per day (Smith *et al.*, 1998). Of the recruits to the Secker-Walker trial, the mean number of cigarettes was 22.2 cigarettes per day (Secker-Walker *et al.*, 1989). These figures are both higher than the smoking levels in this trial. Macgregor (1996) did not report mean cigarette consumption from his cohort, only that they had to smoke at least five cigarettes to be included in the trial.

The *Scottish Health Survey 1998* reported mean numbers of cigarettes smoked per day of 17.5 for men, and 15 for women (Shaw *et al.*, 2000). Thus, generally, trial

participants smoked at the same or slightly higher levels than those surveyed in the SHS 1998.

Of the trial participants, only 17% smoked within the first 30 minutes of waking. In contrast, in the Smith trial, 76% smoked within the first half hour of waking (Smith *et al.*, 1998). Therefore, for this element of the FTND, the Glasgow group exhibited less addiction than the participants in the Smith trial.

4.4.3.6 Environmental Exposure to Smoke at Home and Work

Over one third (39%) of the study participants were exposed to smoke at home. It is known that trying to quit when there are others smoking in the vicinity can be difficult, and individuals are less likely to succeed in these circumstances (Health Scotland and ASH Scotland, 2004).

Half of all trial recruits (52%) were exposed to smoke at work. Once again, such exposure will tend to make quitting more difficult.

Environmental tobacco smoke, especially in the workplace, is a topical issue in Scotland, with a public consultation currently underway, relating to banning smoking in public places. The Scottish Executive is seeking the public's views with regard to restriction or prohibition of smoke in enclosed public places. This could take the form of a total ban (as in force in Ireland from 2004) or a targeted ban on smoking in specific places such as hospitals and schools, or where food is served (Scottish Executive, 2004b). Other options would be to give powers to local authorities to regulate smoking in public places, or a combination of statutory controls and voluntary action.

4.4.3.7 Lifetime Exposure to Cigarette Smoke

With regards to lifetime exposure, patients were asked how many years they had smoked, and with information accrued from the number of cigarettes smoked, pack-years were calculated. The mean number of pack-years was 23.1, with a range of two to 74. There was a difference of 3.3 in mean number of pack-years between intervention and control, with the control group having a slightly higher exposure. This difference was within acceptable limits, and related to the slightly higher mean age of the control group.

Only one of the previous dental smoking cessation studies reported pack-years (Secker-Walker *et al.*, 1988), with an average of 29.5 pack-years for the 51 participants in that trial. Therefore, the participants in the Glasgow trial exhibited a slightly lower mean level of lifetime exposure than the participants in the US study.

The lack of use of the measure of pack-years in the dental smoking cessation literature is surprising, considering there is widespread use of pack-years in periodontal research (Grossi *et al.*, 1995; Mullally *et al.*, 1999; Haffajee and Socransky, 2001).

4.4.3.8 Measures of Motivation to Quit at Baseline

Two measures of motivation to quit were obtained: Motivation Score (Foulds, 1996) and an adapted form of the 'Stage of Change' (Prochaska and DiClemente, 1983, 1993).

a) Motivation Score (Foulds)

With respect to the Motivation Score (Foulds, 1996), two questions contributed to this, both measuring strength of desire to quit ('How much do you want to give up altogether', and 'Would you give up smoking, if you could do so easily'). Both scales were added together to give a total score. The use of this Motivation Score by Foulds proved to be of limited use, as most participants (71%) had a score of seven or eight and professed interest in quitting. The scale was not sensitive in teasing out who would quit, and who would not. None of the previous dental trials used this Motivation Score in their data collection forms.

b) 'Stage of Change'

At baseline, 13% of the sample recruited to this trial were not interested in quitting ('precontemplators'), 45% were thinking about quitting sometime in the next six months ('contemplators') and 42% wanted to stop sometime within the next month ('preparation' stage). This reflects a lower percentage of 'precontemplators', and a higher percentage of smokers in the 'preparation' phase, than in other studies (Butler *et al.*, 1999).

Regarding the high level of individuals in the 'preparation' stage, as already discussed in Section 4.3.3.3, the definition of the stages can vary, particularly in relation to the 'preparation' stage. A number of researchers define those individuals as being in the 'preparation' stage if they want to quit within one month, and have had a quit attempt in the last year (Prochaska and DiClemente, 1983; Prochaska and Velicer, 1997; Etter *et al.*, 2003). Others, however, define the 'preparation' stage solely as wanting to quit within the next month (Foulds, 1996; Butler *et al.*, 1999; Hughes *et al.*, 2000; Etter and

Perneger, 2001). With respect to this current study, the definition of wanting to quit within the next month was used alone, i.e. it did not include whether a quit attempt of at least 24 hours had been made in the last year. This would have led to a higher number of participants being allocated to the 'contemplation' phase, rather than the 'preparation' stage.

Population surveys of smokers would indicate that 40% of smokers are in the 'precontemplation' phase, 40% in the 'contemplation' stage and 20% in the 'preparation' stage (Velicer *et al.*, 1995). None of the dental studies reported using 'Stage of Change' as a measure at baseline. However, many asked about intention to quit, with one asking as a 12-month outcome, about intention to quit within the next 30 days and whether a quit attempt in the last year had been made (Severson *et al.*, 1998).

With respect to other smoking cessation studies, in a UK general medical practice, 53% and 49% of the 'brief advice' and 'motivational consulting' groups were 'precontemplators', 23% and 28% were 'contemplators', with 9% and 10% respectively being in the 'preparation' stage (Butler *et al.*, 1999). This is a much higher level of 'precontemplators' than in the Glasgow study, with a much lower number of participants in the 'preparation' stage. The same definition of 'preparation' was used in the two studies, so the differences between these two studies are not due to variation in definition of the different stages. It may be that the populations were not similar enough for comparison, i.e. a group attending general medical practice in a primary care setting and a group attending a Periodontology clinic in a dental secondary care setting.

One study, looking at assessing 'Stage of Change' in smokers, found that including previous quit attempts in the classification of smokers in the 'preparation' stage had quite an impact, in that 18-24% of smokers were downgraded to 'contemplation stage' as they had not made a quit attempt in the last year (Etter and Sutton, 2002). When looking at the present study, if this method of analysis had been used, 30% of the participants categorised as 'preparation', would be downgraded into the 'contemplator' category.

Etter and Sutton (2002) criticised the definition of including quit attempts within the categorisation of the 'preparation' stage, and concluded that with such an inclusion, the 'contemplation' stage becomes a heterogeneous category that encompassed smokers wanting to quit in the next 6 months, and who may/may not have had a quit attempt, and smokers who want to quit within the next month but have not made a quit attempt.

Etter and Perneger (1999) compared two measures of 'Stage of Change', using a conventional questionnaire and a shortened, easier to interpret version, and found that only 62% of participants were classified in the same stage through use of the two questionnaires. Thus, variations in questionnaire design can make comparing results from different studies difficult and in some cases, not valid.

Researchers have also looked at 'Stage of Change' test-retest reliability, and found that over a 7-day interval, 16% of 'precontemplators' and 6% of contemplators progressed to the next stage, and 33% of those in the 'preparation' stage regressed to 'contemplation' (Hughes, 2001). Etter and Sutton (2002) found a similar, if less marked change, in their study with 15% of participants changing category over an 8-day

period. Therefore, it is postulated that there is a certain fluidity in this model, and this must be acknowledged.

As mentioned previously, the 'Stage of Change' is only one element in Prochaska's Transtheoretical Model of Change. Other elements include processes of change, decisional balance, and self-efficacy (Prochaska and DiClemente, 1983). Use of these elements would have required additional data collection, and as such, was outwith the scope of this thesis.

4.4.3.9 Cotinine and Carbon Monoxide Levels at Baseline

Recruitment into the trial was by self-reported daily smoking of at least 10 cigarettes per day. No individual was recruited into the trial who was currently trying to quit, or was taking NRT.

When the results of cotinine analysis became available a number of months after patient recruitment, it was found that two individuals had cotinine levels below the cut-off, one intervention and one control. Both cases had, however, CO concentrations well above the cut-off level. One individual (intervention) was lost to follow-up at 3 months. The other participant (control) had biochemistry indicative of more regular smoking at this time point.

While it could perhaps be argued that the low cotinine levels measured at baseline for these two individuals, should have resulted in them having being excluded from the study, given their relatively high CO levels, the decision was made to include these individuals in the analysis.

4.4.4 Patient Follow-ups at 3, 6 and 12 Months

With respect to follow-ups, data were collected from 88% of participants (both intervention and control) at 3 months. This very acceptable rate was due to the patients still largely being under periodontal treatment by the dental hygienists, and this considerably aiding the collection of follow-up information. Severson *et al.* (1998) reported a follow-up rate of 75.7% at this time point, with Macgregor (1996) reporting a 3-6 month follow-up rate of 88%.

With respect to the 6-month follow-ups, the rate reduced to 61% for both intervention and control groups. Obtaining patient data at this time point proved to be more challenging, especially for those patients who had finished attending the Periodontal Department. Some patients had been referred internally for further treatment, and it was possible to obtain follow-up data within the specified timeframe during their attendance at other departments within the hospital. Other patients who were not returning within the specified timeframe were contacted, and it was requested that they attended the research hygienist solely for collection of data.

Cohen *et al.* (1989) had a follow-up rate of 42% at this time point, with Secker-Walker and co-workers (1988) obtaining data from 94% of their original sample. In this latter study, telephone interviews were used to collect data and patients did not have to attend in person for any biochemical verification.

With respect to one-year follow-ups in this study, there were much-reduced rates of 56% in the intervention group and 40% in the control group, with the overall rate being 48%. The data collection methodology was different at this time point, utilising

telephone and postal follow-ups. Whereas telephone data collection had yielded a very respectable rate of 94% follow-up at six months in the trial described by Secker-Walker and colleagues (1998), this means of data collection was not so successful in this trial, albeit at the much longer time-frame of one year. By this time, a large proportion of subjects had completed their treatment and were no longer current patients of Glasgow Dental Hospital.

At one-year, Severson *et al.* (1998) had a follow-up rate of 75.7% (same as at 3 months). This was a large well-funded trial with dedicated staff to help with patient follow-ups, and this is reflected in the impressive follow-up rate at one year.

Other trials have reported similar problems to the present study, concerning attempts to obtain follow-up data. Cohen *et al.* (1989) had 36% of the original participants return at the one-year time point. Smith *et al.* (1998) reported data at the 9-month time frame on 48% of the original recruits to the trial. Therefore, the 48% follow-up rate achieved in the present study compares favourably with most other dental smoking cessation trials.

4.4.4.1 Primary Outcomes of Smoking Cessation

Primary outcomes of smoking cessation were determined at 3, 6 and 12 months, biochemically validated. As previously discussed, the date of the follow-up was related to the date of the collection of the patients' baseline data, rather than the date of any quit attempt. Previous dental smoking cessation interventions have looked at outcomes at 3 and 6 months, and it was decided to use these time points, as well as the longer-term outcome of one year.

4.4.4.2 Three Month Outcomes

Point prevalence outcomes indicated that, of those individuals followed up at three months, 17.3% (9) of participants were classified as quitters in the intervention group, compared to 10.0% (5) in the control group. Assuming all patients lost to follow-up were still smoking, of the patients recruited at baseline, 15.3% (9) in the intervention group quit, compared to 8.8% (5) in the control group.

The situation at 3 months is complex, as described in Table 3.33, with a number of quitters still using NRT and this being reflected in the cotinine levels. One ‘deceiver’ was identified, and one individual whose biochemistry was more indicative of a non-smoker, was also identified.

Of interest is the number of control participants who, at the time of data collection, were in the process of quitting. Two of the control group were disappointed at being allocated to the arm of the trial where no help was given, and as such, wrote comments on the three-month data collection forms.

Patients recruited to such trials have to show informed consent, and as such, receive information as part of the recruitment process. In this study, the information sheet included not only details of the trial, but also information about periodontal disease and the role that smoking can play in exacerbating the condition. This, in itself, would almost constitute a ‘brief intervention’, even in the absence of any further advice and help. This, together with the ‘usual care’ advice that all smoking patients newly referred to the Periodontology Department receive, encouraged at least some of the control group to help themselves or to seek further support, as evidenced by the use of the NRT.

Severson and co-authors (1998), in their large study of both smokers and individuals using smokeless tobacco, linked the date of follow-up to the date of enrolment (as in the present study). The sample sizes in each of the treatment groups were approximately 20 times the sample sizes in the present study: 'usual care' had 1,350 patients enrolled, with 1,305 and 1,374 in 'minimum' and 'extended' interventions respectively. At 3 months, it was found that in the 'usual' care group, 63 (4.7%) had quit, compared with 66 (5.1%) in the 'minimal' intervention and 77 (5.6%) in the 'extended' intervention group. This study relied on self-report and did not use any form of biochemical validation.

Macgregor (1996) followed up his patients at variable timeframes between 3 and 12 months. Of the 38 patients who were given dental health advice only, 5.4% had quit, while 13.3% of the 98 patients who were also give advice to stop smoking had quit.

At the three-month time point, with a quit rate of 15.2% in the intervention group, compared to 8.8% in the control group, the success of the present trial with respect to the intervention group is similar to that of Macgregor and in excess of that reported by Severson *et al.* (1998). The results are not statistically significant, but indicate a modest, positive effect in the right direction.

It has to be borne in mind that both this trial and the one run by Macgregor (1996), were much smaller with regards to number of participants than the very large trial run by Severson and colleagues.

It should also be noted that the type of intervention may have influenced quit rates. In some studies it was difficult to determine the exact nature of the intervention. Additionally, compared with some other types of randomised controlled trials, e.g. drug trials, smoking cessation studies will have more variation in relation to the specific content of the intervention and the individual delivering the intervention is also likely to have a larger impact.

4.4.4.3 Six Month Outcomes

Point prevalence outcomes of those followed up at 6 months, indicated that 16.7% (6) of participants were classified as quitters in the intervention group, compared to 8.6% (3) in the control group. Assuming all patients lost to follow-up were still smoking, of the patients recruited at baseline, 10.2% (6) in the intervention group quit, compared to 5.3% (3) in the control group. Prolonged abstinence figures (based on patients followed-up / total patients recruited) would indicate that 11.1% / 6.8% of the intervention group had quit, compared to 8.6% / 5.3% of the control group. In this study, prolonged abstinence was defined as those quitters at 6 months, who had also been classified as quitters at 3 months.

Two patients were still using NRT at the 6 month time point, and this was reflected in their cotinine levels. With many studies, the longer the period of follow-up, the lower the success rate, as individuals relapse. This occurred in this study, with a lower quit rate being found at 6 months, compared to 3 months.

Secker-Walker and co-workers (1988) included six-month outcomes (point prevalence) in their trial of 51 smokers and data are reported on the 48 individuals who provided

information at this time point. It was reported that seven (14.6%) trial participants stated that they had quit. Information was collected by telephone interview. The comparable figures for this study (i.e. reported on the basis of those followed-up), reports a success rate of 16.7%, so the Glasgow study exhibits similar results to those of Secker-Walker and colleagues. It has to be stressed that this latter trial used no biochemical validation and therefore, results may be slightly inflated.

In a trial by Cohen *et al.* (1989) using ‘gum’, ‘gum and reminders’, ‘reminders’ and a control group, findings were reported on both individuals followed-up and numbers recruited at baseline. The authors do not state what measure they use, but it would appear to be point prevalence. The arm of the trial most closely resembling the 5As and NRT intervention group in the Glasgow study would be the ‘gum and reminders’ group. The success rates for patients quitting (reported as patients followed-up / total patients recruited) in Cohen and co-workers trial were 9% / 3%, compared to 16.7% / 10.2% in the Glasgow trial. Therefore the findings of the present study would indicate a higher level of success.

The one UK trial in general dental practice collected 9-month outcome data (measured from the patients’ registration), and the findings were biochemically validated by cotinine (Smith *et al.*, 1998). Of the patients recruited at baseline, 11% (17 patients) had quit at the 9-month point. This trial was not of an RCT design, so there are no control findings to report. Using the six-month figures from this PhD study, and with the findings calculated from all patients recruited at baseline, 10.2% of the intervention group quit, a finding similar to that of Smith and co-workers.

Evidence from smoking trials in general, (i.e. not restricted to the dental setting) would indicate that an intervention utilising various forms of NRT with limited or intensive behavioural support, normally yields a success rate of between 5% and 12% at 6 months (Appendix 12). This table reports results as the difference between the intervention and control groups, with the control group being defined as willpower or placebo, or as no intervention. With a success rate of 10.2% (of all patients followed-up) in the intervention group, compared to 5.3% in control group (usual care), this project is within the expected limits of success.

With regards to the prolonged abstinence results of this study, it was not possible to find comparable dental literature to make valid comparisons, due to differences in the way the results have been collected. It was also not possible to compare the findings with results from specialist smoking cessation services as neither England nor Scotland collects data at this time point.

Therefore, the reporting of success in smoking cessation trials can be subject to variances not only in methodology regarding the different interventions, but also to how the results are reported at the varying time points and whether biochemical validation was used.

4.4.4.4 Characteristics of 6 Month Quitters

Descriptors of the 6-month quitters (Tables 3.46 and 3.47) would indicate that all were women. As the trial participants were predominately women (71%), this finding is not entirely unexpected. It is known that women attend for regular dental treatment more

readily than men, and are more likely to see the benefit of preventive treatment, and within this setting, these more positive health beliefs may have played a role.

With respect to all quitters, seven out of nine came from DEPCATs 1-4. As with many smoking cessation trials, individuals who are from the less deprived areas, tend to be more successful at quitting (Bauld *et al.*, 2003; Jefferis *et al.*, 2004).

When looking at the data and translating the age of the participants and the number of years smoked into the age of starting smoking, one issue becomes clear. All the quitters started smoking between the ages of 14 and 20. Individuals rarely start smoking after their early twenties (Dobson, 2004). Picking up the tobacco habit very often occurs during the teenage years, and this is why, over the last decade, much effort in both research and development has been expended in trying to provide services for young people, in an attempt to enable them to quit before they are truly addicted.

4.4.4.5 Relapse Rates at 6 Months

With respect to the relapse rate at 6 months, six of the 3-month quitters had relapsed back to smoking. Relapse can be defined as a return to regular smoking on seven consecutive days, as opposed to a lapse whereby an individual may have a single cigarette (Hughes *et al.*, 2003). Some researchers feel that a lapse back to smoking within the first week of quitting can be indicative of failure to quit in the longer term (Kenford *et al.*, 1994), while others feel that many smokers do have lapses very early on in the first few days, but may become abstinent between the 3 and 6 month mark (Hughes *et al.*, 1992).

Patients in this study may have found it relatively easy to have a quit attempt (Section 4.4.4.2), but sustaining that quit is challenging for individuals.

Relapse prevention is an important factor in smoking cessation. The topic of relapse prevention interventions for smoking cessation is currently the subject of a Cochrane protocol (Hajek *et al.*, 2004). In this protocol, Hajek and co-authors state that multisession behavioural programmes should include relapse prevention components which aim to help smokers identify triggers or high risk situations for relapse, and give them advice and strategies for coping and avoidance.

Self-help manuals and patient information often include tips about how to avoid relapse, and the information given to the patients in the current trial included these strategies (Smoking Concerns, 2004). Future studies may be required to evaluate what help or support recent quitters need to sustain their quit attempt.

4.4.5 Pharmacological Support during the Trial

Of the participants who were successful at quitting at 6 months, all made use of pharmaceutical support. Most made use of NRT (eight participants), with one individual using Zyban. These results indicate that use of NRT in a smoking cessation project in a dental setting is a key issue. The evidence for the effectiveness of NRT is now substantial (Silagy *et al.*, 2004), and access to its use is considered a key strand of smoking cessation therapy (Health Scotland and ASH Scotland, 2004). While there may be no doubt as to its efficacy, there is controversy over where it may be given out and who pays for it.

Within this trial, NRT was freely available for those participants allocated to the intervention group who wished to use it. The costs, as previously discussed, were borne by *Smoking Concerns*. This is not the situation that is currently available in other dental settings, or indeed the normal practice in the dental hospital in which this study was located.

At the moment, dentists are not able to prescribe NRT or Zyban. However, this will change with the imminent abolition of the *Dental Practice Formulary* guidelines, allowing dentists to prescribe anything in the *British National Formulary*, including NRT. Guidance exists for the use of NRT both in Scotland and England (HTBS, 2002; NICE, 2002). As smoking is firmly implicated as a risk factor in periodontal disease and oral cancer, it would not seem unreasonable to allow dentists to prescribe effective medication in the form of NRT regarding tobacco dependence treatment. This, however, would involve the presumption that dentists have the appropriate knowledge and confidence to do so. There are no plans to allow dental hygienists to have the right of prescribing. Therefore, if they wish their patients to have NRT in the near future, it would need to be in conjunction with dentist prescribing.

Another mechanism exists for prescribing and this is known as a *Patient Group Direction*. It was originally set up for use by pharmacists to allow them to supply NRT as part of their smoking cessation interventions, as well as enabling distribution via NHS smoking cessation advisors, who cannot prescribe under normal circumstances. The aim was to prevent unnecessary visits to the family medical practitioner, to obtain supplies of the NRT product. However, in practice, it is a cumbersome system to set up and administer, and would probably be of limited value to the dental profession.

One further option exists for patients to gain access to NRT, and that is they purchase it over-the-counter, bearing the costs themselves. Dental team members could raise awareness of the differing types of NRT, and suggest that they seek further information from the pharmacist.

4.4.6 Primary Outcomes at One Year

Point prevalence outcomes of those followed-up at one year, indicated that 12.1% (6) of participants were classified as quitters in the intervention group who were followed-up, compared to 8.7% (3) in the control group. Assuming all patients lost to follow-up were still smoking, of the patients recruited at baseline, 6.8% (6) of the intervention group quit, compared to 3.5% (3) in the control group.

For the intervention group, this was slightly better than the results reported (for all patients recruited at baseline) by Severson *et al.* (1998), who found a quit rate of 2.4%, 2.6% and 2.5% for 'usual care' 'minimal', and 'extended' interventions respectively, at 12 months.

The trial by Cohen *et al.* (1989), already discussed in relation to the six-month findings, also reported at one year. At this time point, Cohen reported the findings on both individuals followed-up and numbers recruited at baseline. As already specified, the arm of the trial most closely resembling the 5As and NRT intervention group would be the 'gum and reminders' group. The success rates for patients quitting (reported as patients followed-up / total patients recruited) for Cohen's trial were 16.9% / 4.7%, compared to 12.1% / 6.8% in the Glasgow trial. Therefore, the findings for the Glasgow trial would indicate a slightly lower level of success.

Neither of the previously described trials (Cohen *et al.*, 1989; Severson *et al.*, 1998) used biochemical validation, so results quoted are purely self-report and may be subject to inflation. The Glasgow trial, used not only self-report, but also cotinine biochemical verification, so very stringent measures were used to define success. At the 3 and 12 months time points, 'deceivers' were detected in this trial, and Smith and co-workers (1998) also found two deceivers, as verified by cotinine. Therefore, it would not be unreasonable to assume that the other trials would exhibit some degree of over-reporting of success.

4.4.7 Secondary Outcomes - Changes in Smoking Behaviour at 3 and 6 Months

4.4.7.1 Quit Attempts

At 3 and 6 months, trial participants who still smoked were asked whether there had been any changes in their smoking behaviour, including quit attempts of varying duration. At both time points, there was a statistically significant higher percentage of individuals in the intervention group than control who reported that they had made a quit attempt of one week or more in the preceding 3 months: 37% and 47% at 3 and 6 months respectively for the intervention group, compared to 18% and 16% respectively for the control group. This would indicate that the intervention was successful in encouraging relatively high numbers of smokers to try to have a quit attempt of at least a week.

Severson *et al.* (1998) collected secondary outcomes at 1 year, and found that 41% of the 'extended' intervention had made a quit attempt during the period of the trial. None of the other dental interventions collected this information.

It has been reported that having successful quit attempts, albeit if the patient relapses, helps increase patient self-efficacy, increasing the likelihood that the patient will be successful in the future (Borland *et al.*, 1991; West *et al.*, 2001).

In this study, secondary outcomes were not collected at the one year mark, due to the differing data collection methodology used, i.e. telephone and postal collection. It was decided to focus on primary outcome measures at this time point, to make the information collected brief, in an attempt to aid the response rate.

4.4.7.2 Smoking Reduction

At 3 months, 81% (35) of the intervention group reported they had reduced their cigarette intake in the past 3 months, compared to 45% (20) of the control group, and this was statistically significant. At 6 months, however, the difference between the groups was not statistically significant, with 67% (20) of the intervention group having reduced their cigarette intake in the previous 3 months, compared to 56% (18) of the control group.

Most dental trials undertaken to date, have not collected information on smoking reduction (Cohen *et al.*, 1989; Severson *et al.*, 1998; Smith *et al.*, 1998). The Macgregor trial did, and found that 67% of those given smoking cessation advice claimed to have reduced their smoking in some way.

There are two aspects to smoking reduction, the first behavioural and the second, physiological. Some researchers feel that advocating smoking reduction is swaying smokers away from the real task of quitting (Fiore *et al.*, 2000), whereas others feel

from a behavioural point of view, smoking reduction may be a stepwise approach to quitting (Carpenter *et al.*, 2003).

Most public health strategies do not recommend promoting or reporting on reduced smoking among smokers who are trying to quit (Fiore *et al.*, 2000). There is some evidence that smokers are able to titrate as much nicotine from a reduced number of cigarettes by altering their smoking patterns and inhaling more deeply (Hughes *et al.*, 1981).

In contrast, Hughes (2000), in his review of reduced smoking, found that there were reductions in CO exposure ranging from 19% to 35% in participants who claimed to have reduced their percentage cigarette intake.

More recent work by Carpenter and co-workers (2003) in a cohort of smokers not interested in quitting but willing to reduce, found that of smokers who were encouraged to reduce their number of cigarettes to 50% of their usual intake by week four, 71% were able to reduce their intake by at least 33% and were able to maintain their reduction 6 months into the trial. The authors concluded that reducing smoking neither prompted nor undermined smoking cessation. In addition, they postulated that for some hardened smokers, smoking reduction may be an intermediate step, as it would help decrease withdrawal severity, urges for cigarettes and increase patient self efficacy, which should, in theory, help the future likelihood of a successful quit attempt. It has to be stressed that this work utilised CO with its short life, and it is postulated that using cotinine would have given more detailed results.

In the study reported in this thesis, information was elicited from the individuals regarding whether they had reduced their smoking or not, and this was related to their cotinine levels at baseline, and at 3 and 6 months. The results showed that not all individuals who claimed to have reduced the number of cigarettes smoked reduced their nicotine loading, and in some instances, a reported reduction in number of cigarettes smoked was associated with an increased level of cotinine at 3 and 6 months compared to baseline. However, at 6 months, a significantly higher mean cotinine reduction 61 (SD 90)ng/ml was seen in the group who reported reducing their smoking.

As there is a dose-response seen regarding number of cigarettes smoked and the severity of periodontal disease, if smokers manage to reduce smoking and maintain it at low levels, there may be some benefit from a 'harm reduction' point of view. Tomar and Asma (2000) found that smokers who reduced the number of cigarettes from over 30 a day to less than 10, subsequently reduced their likelihood of developing periodontitis (OR = 5.8 to 2.79). Other health professionals are reluctant to countenance any safe level of smoking (Fiore *et al.*, 2000).

In summary, there is debate at present, as to the benefits of smoking reduction, either from a 'harm reduction' perspective, or as the first step on the road to quitting for heavily addicted smokers.

4.4.7.3 Changing to a Low Tar Brand

At the 3-month mark, 22% (28% intervention and 16% control) of trial respondents self-reported moving to low tar cigarettes. At the 6-month time point, 34% (40% of intervention and 28% of control) claimed to have changed within the last 3 months to low tar cigarettes. No advice was given to the participants to change to lower tar cigarettes.

This question was included in the questionnaire as this behaviour is often cited by lay individuals as a means of changing or reducing smoking behaviour. It is postulated that its inclusion in the questionnaire may have 'legitimised' this behaviour, and therefore prompted a higher than expected number of trial participants to take this course of action.

Current theory is that there is no benefit from using light or low tar cigarettes. The marketing of such cigarettes as being 'the healthier option' has recently been banned in the UK and cigarettes have had to have 'light' and 'low' removed from their titles. Smokers are able to titrate just as much nicotine from 'light' cigarettes, and indeed smoking in such a way is thought to contribute to an increased risk of lung adenocarcinoma (Etter *et al.*, 2003). Previous research showed that branding cigarettes as light, appealed to smokers who were younger, female and smokers with a lower nicotine addiction score (Etter *et al.*, 2003).

Hyland and co-workers (2003) looked at the concept of whether switching to a low tar cigarette increased or decreased cessation behaviour. In a retrospective study, looking at participants in a Community Intervention Trial for Smoking Cessation (COMMIT), it

was found that 19% of regular smokers switched to a lower yield product over a two-year period. In this sub-group, despite a greater desire to quit than amongst those smoker who did not change, switching to a low tar cigarette did not appear to increase or decrease the likelihood of future cessation, though motivation to stop smoking may be associated with switching.

4.4.8 Movement in Stage of Change at 3 and 6 Months

‘Stage of Change’ data can be used in two ways. Firstly, it can be used as a ‘predictor’ of outcome and the outcome in this case would be smoking cessation. Secondly, it can be used directly as an ‘outcome measure’, where the participants’ self-reported movement through the cycle is enumerated, in relation to whether they received the intervention (5As and NRT) or control (usual care).

With respect to the former use, i.e. as a predictor of outcome, data collected on the participants’ self-assessment of readiness to change at baseline, was used to examine whether those who said they were in the most ready state, i.e. wanting to stop smoking within the next month (‘preparation’) actually took action and went on and quit.

Of the 14 biochemically validated quitters at 3 months, at baseline nine (64%) had classified themselves as wanting to stop (‘preparation’), four were ‘contemplators’ and one was not interested in quitting (a ‘precontemplator’) (Table 3.39). In contrast, of the 88 participants who were still smoking at 3 months, only 33 (38%) had described themselves as being in the ‘preparation’ stage and 12 (14%) were not interested in quitting. However, with such small numbers, all results have to be interpreted with caution.

At six months, a number of quitters (seven) had moved on to the 'maintenance' phase (i.e. quit for at least six months) and six had relapsed (Table 3.53). There would not appear to be any direct relationship between the 'Stage of Change' at baseline and outcomes at six months.

With respect to looking at 'Stage of Change' as an outcome measure, where 'success' would be considered as positive movement through the model itself, it was expected that those in the intervention group would perhaps have shown an increased rate of forward movement. It was hoped that the smoking cessation advice given to the intervention group would enable them to think more positively about stopping smoking, even if they did not quit.

At 3 months, there was little difference between intervention (14) and control (15) for those who moved forwards (Tables 3.40 and 3.41). There were slightly more who moved backwards in the control group (12) than for the intervention group (7). With respect to the 6-month results, there were slightly more participants in the intervention group who moved forward (13), compared to the control group (7), suggesting a potential slight benefit from being allocated to this group. However, once again, with relatively small numbers, it is difficult to form any firm conclusions.

None of the dental trials used 'Stage of Change' as a predictor in their study. One study, however, used it as a secondary outcome measure at 12 months (Severson *et al.*, 1998). The authors reported that there was a statistically significant difference between the number of participants in the 'extended' intervention group, who claimed that they wanted to quit in the next month, compared to the 'usual care' group.

Butler and co-workers (1999) used 'Stage of Change' in a trial in general medical practice, reporting patients' self-reported intention to quit at both baseline and 6 months. No analysis of any movement of the 'Stage of Change' was undertaken although the numbers of participants in each 'Stage', at both baseline and 6 months, were reported. There was a greater reduction between baseline and 6 months in the percentage of participants who claimed to be not interested in quitting in the 'motivational consulting' group compared to the 'brief advice' group. Between baseline and six months there was little change in the proportion of participants claiming they wanted to quit within the next month, with similar proportions in the two groups.

Butler and co-workers also used the baseline 'Stage of Change' to examine whether there was the same benefit of 'motivational consulting' over 'brief advice' for participants who were not interested in quitting at baseline ('precontemplators') compared to participants who showed some interest in quitting ('contemplation', 'preparation' and 'action'). The analysis showed that the additional effect of 'motivational consulting' over 'brief advice' was significantly greater for participants who were classed as 'precontemplators' at baseline, in terms of self-reporting a quit attempt and reducing smoking. There were similar results, although not statistically significant, with regard to not smoking in the previous month, not smoking in the previous 24 hours, two or more quit attempts and a quit attempt of at least one week's duration (all self-reported).

It is emphasised that the present study was experimental pilot usage of 'Stage of Change' in a dental setting. This had not been attempted before. Future work should include validating the questionnaire or finding another validated instrument, and further

developing meaningful analysis of the data collected. Options could include reanalysing the data, using a different definition for 'preparation stage', and analysing the results in the manner described above by Butler *et al.* (1999).

4.5 Smoking Cessation and the Dental Team – the way forward

4.5.1 Secondary Care

The work of this thesis has shown that, given training in smoking cessation and access to NRT for their patients, dental hygienists, working in a secondary care setting, can have a modest effect, with regards to the provision of smoking cessation, at least in line with success rates reported by other health professionals (NHS Health Scotland and ASH Scotland, 2004).

Research has shown that hygienists tend to be more favourably disposed to the topic of smoking cessation than dentists (Fried and Rubenstein, 1990, Halling *et al.*, 1995; Gussy *et al.*, 1996; Syme *et al.*, 2001). Dental hygienists are also more likely than dentists to routinely advise their patients to quit smoking (Fried and Rubenstein, 1990; Chambers and Corbin, 1996; Nicotera *et al.*, 2004), and are more likely to be proactive in assisting their patients (Chambers and Corbin, 1996; Helgason *et al.*, 2003). Therefore, of the dental team members, it would appear that dental hygienists may be the most appropriate group to take this topic forward.

Given the results of the present study, consideration should be given to developing smoking cessation services provided by trained dental hygienists, within a dental secondary care setting. This would be particularly relevant within Periodontal clinics, where patients attend for multiple treatment sessions. During hygiene phase therapy,

smoking advice can be integrated into the patient's relevant clinical care. In the present study, dental hygienists also discussed NRT with the patients and gave those who requested it, supplies of nicotine patches and gum. A contemporaneous trial running in a hospital periodontal department, in addition to using NRT, successfully utilised Zyban for patient support (Heasman *et al.*, 2004). This trial found a quit rate of 40.5% among all participants at 3 months. As this work is very recent, it has yet to be reported in the form of a full peer-reviewed publication.

Therefore, potential developments within this field would include investigation of methods available for the provision of appropriate pharmacological support, including NRT and Zyban.

Within the restorative discipline, dental implant patients constitute another group who could benefit from smoking cessation advice. It is known that the implant failure rate is much higher in those who smoke (Bain, 2003). This author has been successful in promoting smoking cessation with this group. When looking at smoking cessation outcomes at 3 months, 6 months and 1 year, the success rates were 70.2%, 43.9% and 40.4% respectively (Bain, 2003). However, these outcomes were not biochemically validated by cotinine.

These high cessation rates, no doubt, reflect the motivated individuals who were carefully counselled as to the potential higher success rate if they quit smoking. Counselling included details about the patient's responsibilities for achieving the best prognosis, coupled with the information to cover the clinician in the event of implant failure in the non-compliant patient. It would seem unrealistic to translate these high

cessation rates into any other dental setting except, perhaps, for oral cancer/pre-cancer patients and success of smoking cessation programmes with this group is currently unevaluated.

Thus other settings where advice and help regarding smoking cessation should be considered, are outpatient Oral Medicine/Oral Surgery clinics. In such settings, patients are referred with potentially malignant lesions, with tobacco as a key risk-factor. Patients may not attend such clinics as frequently as those in Periodontal departments, with treatment planning influenced by their diagnosis. Therefore, patient treatment and follow-up may present more of a challenge, compared to the more structured and regular-attending periodontal patients.

Patients who are diagnosed with oral cancer and who smoke, constitute a specialised target group for whom a sensitive, individualised approach will be required. Further research is required to determine which methodology, with respect to smoking cessation, is the most appropriate to be used with this group.

The dental hygienists who undertook this study were trained in various aspects of smoking cessation and were highly motivated. The outcome of future work carried out within dental secondary care settings will be dependent on the intervention used and the training and level of motivation of those delivering the smoking cessation intervention.

4.5.2 Primary Dental Care

With respect to smoking cessation policy in Scotland, two recently released documents both acknowledge the role that dentistry, within the primary care system, can play in smoking cessation (NHS Health Scotland and ASH Scotland, 2004; Scottish Executive, 2004a). However, it is perhaps disappointing that neither of these recent publications mentions dental hygienists or other professionals complementary to dentistry, with the only reference to dental team members being to the 'dentist', or 'general dental practitioner'. Guidance from the Scottish Executive (2004a), states that....'GPs, practice nurses, midwives, **dentists**, pharmacists, health visitors, and other health professionals, all potentially have a role to play in giving smoking cessation advice. Such advice need not take long, but the messages need to be consistent.' (Scottish Executive, 2004a).

It would appear from recent policy documents that there has been a move away from the previously-cited 'stepped care' approach, the focus of earlier recommendations (ASH Scotland & Health Education Board for Scotland, 2000). In this previous approach, patients were targeted with the least intensive intervention necessary to enable that person to stop smoking. There is now also added emphasis on referral pathways to specialist services (NHS Health Scotland and ASH Scotland, 2004). It acknowledges that there is a ..'...vital role in smoking cessation played by GPs and other primary care staff, **general dental practitioners**, community pharmacists...either in referring patients to appropriated services or, if suitably trained and resourced, providing smoking support themselves'.

This recent recommended approach to smoking cessation, i.e. increased emphasis on referral to specialist services, raises two main issues, the first regarding the referral process itself, and the second point with respect to training and resources. Both of these points will be discussed below.

The move to greater emphasis being placed on a referral system is not restricted to patients from the dental setting, but this mechanism is also recommended for other primary care patients, such as those from general medical practice (NHS Health Scotland and ASH Scotland, 2004). This approach makes the presumption that there are enough places available in the local smoking cessation services to accommodate those clients who wish to seek help. Scotland has 1.4 million smokers, with area prevalence rates influenced by levels of deprivation.

Scotland is not the only country to place additional emphasis on referral to the specialist services as a means of delivering smoking cessation advice. In the US, the *American Dental Hygienists Association* has launched a tobacco cessation initiative entitled 'Ask, Advise and Refer'. This program has a target to increase to 50%, the percentage of dental hygienists that screen their patients/clients regarding tobacco use (including rate, type and amount) by 2006, from a baseline figure of 25% (Syme *et al.*, 2001). The protocol involves **asking** the patient, **advising** the patient, and **referring** the patient for specialist help and advice, depending on what is available in the local US area.

In addition, England have recently (July 2004) released 'Smoking Cessation Guidelines for the Dental Team', outlining a revised form of the '4As', where in addition to **ask** and **advise**, the **arrange** includes arranging referral to the specialist services, and in the

absence of patients wanting to take this course of action, an **assist** can be used where the dental personnel can help the patient set a quit date and provide the patient with more detailed help and assistance (Beaglehole and Watt, 2004).

The second point raised by the NHS Health Scotland and ASH Scotland document, with respect to the delivery of smoking cessation services, is in relation to training and resources. Currently in Scotland, training in all aspects of dentistry for dental team members takes place via the postgraduate/post-qualification course system, administered by NHS Education for Scotland. CPD (Continuing professional development) courses are aimed at dentists, and PCD (Professionals complementary to dentistry) courses are designed to address the training needs of dental hygienists and dental nurses. Both types of course have covered 'Smoking Cessation' as one of their topics on offer, often as part of a day on 'Oral Cancer Prevention', at various locations around Scotland over the last few years. Smoking cessation information also forms part of a distance learning initiative distributed to all dental practitioners (and medical practices) in Scotland as part of an oral cancer prevention and detection initiative (Macpherson *et al.*, 2003).

Training standards for smoking cessation in both England and Scotland have been released (Health Development Agency, 2003; PATH, 2004). English training standards encompass three levels of training, 'brief advice', intensive one-to-one support and group interventions. Scottish training standards outline two levels of input; brief advice and specialist training support. All training developed in the future, including that for all dental team members, will need to encompass the relevant training standards, at whatever level is considered appropriate for each professional.

As previously stated, the current research was undertaken in a secondary care setting, and conclusions can be drawn about its relevance in this context. However, in primary care, with particular reference to primary dental care, other factors including the system of remuneration will influence the applicability of this work.

Currently, in the UK there is no specific system of remuneration for dental health professionals in primary care to provide smoking cessation advice, in any form, to their patients. Thus, even 'brief advice' is considered by most dentists to be outwith the remit of current practice (Watt *et al.*, 2004). This lack of remuneration constitutes a specific barrier to the widespread adoption of smoking cessation advice within a primary care dental setting. Currently the system of remuneration for dental primary care in England is under review, and it is unclear what developments may be forthcoming, with regards to this area, north of the border.

In addition, there would appear to be a lack of clarity at present as to the particular nature and level of the advice, that it would be appropriate for dental team members to deliver, be it 'brief advice', 'brief advice and refer', or more intensive one-to-one support, in appropriate situations. Further research into this area, including a health economics assessment would have to be undertaken.

One study has attempted to look at the feasibility of using a fee for referral to the specialist smoking cessation services. In this pilot project in Sheffield, the equivalent of a check-up fee was given to dentists for referring patients to such specialist services. A successful referral was defined as a patient turning up to a smoking cessation clinic and setting a quit date. Initial evaluation suggested that, compared to other health

professionals such as nurses and pharmacists, dentists were not as successful as identifying patients who could benefit from support (Beaglehole and Watt, 2004). The results would suggest that even at this level of input, further training of dental health professionals is required. There would appear to be no similar pilot projects taking place in Scotland.

As workforce problems deepen with respect to numbers of dentists, both north and south of the border, in some quarters there will be an argument for dentists to restrict their sphere of practice to a more conventional model of delivering dental services, rather than more innovative work such smoking cessation. However, over the next few years in Scotland, there will be an expansion in the numbers of professionals complementary to dentistry, especially dental therapists (NHS Education for Scotland, 2004). With the links so firmly established between tobacco use and both oral cancer and periodontal disease, it would seem a natural progression and extension of the hygienists' and therapists' duties, to give smoking cessation advice to their patients.

However, as previously discussed, a number of issues would need to be addressed, both in terms of level of input, training and particularly with regard to funding. These professionals complementary to dentistry are likely to be the most cost-effective clinical members of the dental team staff to give smoking advice to patients, though as discussed previously, further economic costing would need to be undertaken to confirm this.

4.5.3 Summary

In conclusion, this project has produced evidence of the potential effectiveness of dental hygienists contributing to the field of smoking cessation in a dental hospital periodontal department setting. The contribution that dental hygienists can make in other settings, such as dental primary care, is at present largely undetermined. However, this will be dependent to a large extent on the recommended direction of primary care smoking cessation work in Scotland and workforce and remuneration issues.

Chapter 5 Conclusions and Recommendations

5.1 Conclusions

The aim of this project was to examine the feasibility and efficacy of a smoking cessation intervention, delivered by dental hygienists, in a cohort of periodontal patients attending an outpatient dental hospital department.

This work has shown that it was feasible to recruit patients into a smoking cessation trial of a RCT design, and deliver smoking cessation advice.

With respect to the efficacy, this thesis has shown that, given training in smoking cessation and access to NRT for their patients, dental hygienists can have a modest effect, with regards to smoking cessation, at least in line with success rates reported by other health professionals (NHS Health Scotland and ASH Scotland, 2004). Results in this study were biochemically verified by carbon monoxide and cotinine.

At 3 months, of the patients followed-up, 17.3% of the intervention group had quit, compared to 10.0% of the controls. Of patients recruited at baseline, 15.3% of the intervention group quit compared to 8.8% of controls.

At the 6-month time point, of the patients followed-up, 16.7% of the intervention group had quit, compared to 8.6% of the controls. Of the patients recruited at baseline, 10.2% of the intervention group had quit, compared to 5.3% of the controls. Prolonged abstinence figures would indicate that of the patients followed-up at 6 months, 11.1% of the intervention group had quit, compared to 8.6% of the control group. When

prolonged abstinence is considered in terms of all recruited patients, the corresponding figures were 6.8% of the intervention group and 5.3% of the control group.

At the 12-month time point, of the patients followed-up, 12.1% of the intervention group had quit, compared to 8.7% of the controls. Of the patients recruited at baseline, 6.8% of the intervention group had quit, compared to 3.5% of the controls.

With regards to changes in smoking behaviours, at both 3 and 6 months, for those patients who were not successful in quitting, a significantly higher number of patients in the intervention group self-reported that they had made a quit attempt of one week or more in the preceding 3 months: 37% and 47% at 3 and 6 months for the intervention group, compared to 18% and 16% respectively for the control group. With regards to self-reported reduction in daily cigarettes at 3 months, there was a statistically significant difference between intervention and control groups (33% v 0%). By 6 months, this self-reported difference was not statistically significant.

When self-reported reduction in smoking was associated with reduction in cotinine levels (reduction of smoking between baseline and 6 months), there was a statistically significant higher mean reduction in cotinine in the group who reported reducing smoking, compared to the group who reported that they had not reduced.

With regards to using the patients' self-reported 'Stage of Change' at baseline as a predictor of likelihood of quitting, at 3 months, of the 14 biochemically validated quitters at this point, nine classified themselves as being in the most ready state i.e. 'preparation' stage. Considering 'Stage of Change' as an outcome measure, where

‘success’ is considered positive movement through the model itself, at 3 months, there was no difference between intervention and control groups regarding numbers who moved forward. At six months, there were slightly more individuals in the intervention group who moved forward compared to the control group. However, this was pilot use of this model, and it had never been used in a dental setting previously. With the relatively small sample size involved, it is difficult to draw any firm conclusions about its use. Further work is required to investigate its potential application within this field.

5.2 Limitations of the Project

This project took place in a secondary care dental setting in the West of Scotland, and was delivered by three trained and highly motivated dental hygienists. Using different hygienists both in similar and different settings, such as general dental practice, may have yielded different results. Even within the secondary care dental setting, differing results may occur, depending on the exact content of the intervention and the skills and motivation of the clinician delivering the intervention.

This project was designed from a public health perspective and looked at both the feasibility and effectiveness of smoking cessation within a secondary care dental setting.

Although conducted within a Periodontal Department, it was not designed with a periodontal perspective as the first order priority. A prospective study, focussing on periodontal outcomes and how the smoking cessation process potentially benefits patients’ periodontal health, would have been an important and interesting project. However, a smoking cessation intervention designed to collect meaningful data with respect to periodontal outcomes would have required a larger number of patients to be

recruited, to ensure enough quitters at follow-up, and as such, was outwith the resources available for this project.

The number of participants recruited was relatively small, though of a similar size to some other smoking cessation trials (Macgregor, 1996; Smith *et al.*, 1998). There was some difficulty experienced in attempting to achieve the target of 120 participants at 3-months follow-up, as only 118 were recruited, and it was not possible to extend the recruitment due to time constraints. In addition, it is not known how many patients were approached and refused, as this information was not collected. This would have been difficult to do, as the consultants who recruited the patients are under various time pressures. However, in any future studies, details of the numbers of patients approached should be collected by the researcher, if at all possible.

No health economic analysis of this project has been undertaken to date. This was considered outwith the scope of this PhD. However, information concerning the hygienists' time involvement, success rate of the trial, costs of NRT and biochemical monitoring, including CO and cotinine testing has been collected, thus allowing economic analysis to be conducted in the future. Comparison of the approach used in this study with referral to the specialist services could also be made.

In the US, dental hygienists have been involved previously in the promotion of smoking cessation with patients who use smokeless tobacco (Severson *et al.*, 1998). As stated previously, the target group used in this study was cigarette smokers, with those using other forms of tobacco excluded. Smokeless tobacco, including the forms used by ethnic minorities, is an important public health problem, but addressing the issues

around promoting smoking cessation with this group was outwith the scope of this thesis. Ethnicity was not an element collected as a patient descriptor, but any future smoking cessation work undertaken would collect such information.

5.3 Recommendations and Future Work

5.3.1 Cotinine and Carbon Monoxide Monitoring

It is known that cotinine (COT), with its longer half-life than carbon monoxide (CO), can measure nicotine exposure in both smokers and non-smokers over a longer period of time. Cotinine (COT) is used mainly in research, whereas CO is used routinely in smoking cessation services. An advantage of the use of CO is that values can be fed back to the patients when smoking cessation advice is being given, and hence used as a motivational aid. Other means of using cotinine, with more instant feedback mechanisms, such as the near-patient test, should be evaluated for use within a dental setting.

The relationship of both biochemical measures, i.e. COT and CO, and nicotine dependence, as measured by both *Heaviness of Smoking Index* and *Fagerstrom Test for Nicotine Dependence*, should be evaluated, using the available dataset.

In addition, the specificity and sensitivity of CO and COT should be investigated, with reference to self-report.

5.3.2 Smoking Cessation

5.3.2.1 Further Analysis of Data collected

Further work to identify the significant factors in predicting change in smoking behaviours of participants, for example using classification trees, could be undertaken. Potential predictors would be baseline demographics, smoking habits, level of physiological dependence as measured by the FTND, and motivation to quit. Both primary and secondary outcomes could be examined.

Further analysis with respect to 'Stage of Change' should be undertaken. One aspect would be to carry out analysis using a different definition of the 'preparation' stage, as previously discussed. A further option would be to run an analysis of 'Stage of Change' similar to the methodology of Butler *et al.*, (1999).

5.3.2.2 Development of Smoking Cessation Services

Given the results of the present study, staff within Periodontal Clinics should consider the feasibility of developing smoking cessation services delivered by dental hygienists. A protocol for smoking cessation based on 'brief advice' and utilising a simplified version of patient assessment could be developed.

Other departments such as Oral Surgery/Oral Medicine departments may benefit from the availability of such services, for patient groups such as those with potentially malignant lesions. In addition, other patients such as those undergoing dental implant treatment, may also be a suitable target group. Such developments should include an economic analysis of the cost-effectiveness of such work, involving different models of delivery.

5.3.2.3 Qualitative Research involving Smoking Cessation in a Dental Setting

Qualitative work, using focus group methodology, was undertaken, with the staff dental hygienists who participated in this project. The aim was to determine their perceptions of the delivery of smoking cessation to their patients. Further analysis of this data should be carried out, to elicit the various strengths and barriers they encountered in their work.

There is much questionnaire data available on the perceived roles of dentists and dental hygienists with respect to smoking cessation. However, very little qualitative research has been conducted regarding dental team members' attitudes to this activity. Qualitative work would enable some of the issues associated with remuneration and training to be explored in more depth, and the feasibility of the implementation of different models, be they 'very brief advice and refer' or 'brief advice', to be discussed. Dentists and dental hygienists from both primary and secondary care should be interviewed in depth.

In addition, it would be useful for patients within a dental setting to give their opinions and perceptions on smoking cessation, as delivered by dental team members.

5.3 Dissemination of Results

The results of this project should be disseminated to those developing smoking cessation policy at national and local levels. Dental health professionals should also be made aware of the findings through presentations and publications in peer-reviewed journals.

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Appendix 1

Smoking and Socioeconomic group

Data from the 1998 General Household Survey (UK)

Prevalence of cigarette smoking by sex and socio-economic group: 1976 to 1988, adults aged 16 and over in the UK

Year	1976	1986	1990	1992	1994	1996	1998
Men %							
SEG 1	25	18	16	14	16	12	15
SEG 2	38	28	24	23	20	20	21
SEG 3	40	28	25	25	24	24	23
SEG 4	51	40	36	34	33	32	33
SEG 5	53	43	39	39	38	41	38
SEG 6	58	43	48	42	40	41	45
Women %							
SEG 1	28	19	16	13	12	11	14
SEG 2	35	27	23	21	20	18	20
SEG 3	36	27	27	27	23	28	24
SEG 4	42	36	32	31	29	30	30
SEG 5	41	35	36	35	32	36	33
SEG 6	38	33	36	35	34	36	33

SEG 1 – Professional occupations

SEG 2 – Employers/Manager

SEG 3 – Intermediate/Junior/non-manual

SEG 4 – Skilled manual/own account non-professional

SEG 5 – Semi-skilled manual/personal service

SEG 6 – Unskilled manual

Data from Scottish Health Survey, 1998

Prevalence of cigarette smoking in Scotland, by sex and socioeconomic group:

1995 and 1998, adults aged 16-64

Men %	1995	1998
Professional Occupations	17	14
Managerial/technical	24	27
Skilled non-manual	27	36
Skilled manual	38	40
Partly skilled occupations	46	53
Unskilled occupations	58	48
Women %	1995	1998
Professional occupations	19	9
Managerial/technical	24	26
Skilled non-manual	35	29
Skilled manual	40	36
Partly skilled occupations	47	51
Unskilled occupations	54	59

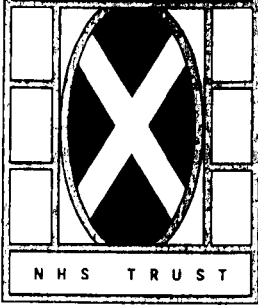
Appendix 2

AREA DENTAL ETHICS COMMITTEE

☎ Direct Dial (Secretary): 0141-211 9796

☎ Direct Dial (Chairman): 0141-211 9855

**GLASGOW
DENTAL
HOSPITAL
& SCHOOL**



HAC/MMcC/02

2 June 1999

Mrs V Binnie
Lecturer in Dental Public Health
Glasgow Dental Hospital

Dear Mrs Binnie

Protocol: The validation of self-reported smoking status by analysing systemic Cofline levels in blood, urine and saliva

I write to inform you that your protocol for the clinic research project has been approved by the Area Dental Ethics Committee subject to:

- an assurance of compliance with the Data Protection Act;
- amendment to the information sheet deleting the word "may" in the sentence commencing "you may already need some blood";
- there should be clarification of the time required for sampling.

The Committee would be grateful if you would inform them of the results of your project and any ethical problems encountered when the project is complete.

Yours sincerely

H A Critchlow
Chairman



378 Sauchiehall Street,

Glasgow G2 3JZ.

Telephone: 0141-211 9600

Fax: 0141-211 9800

Appendix 3

University of Glasgow Dental School

Information Sheet to Patients

Here at Glasgow Dental Hospital and School we are looking at measuring patients' exposure to tobacco smoke in a study entitled:

“The Validation of Self-Reported Smoking Status by Analysing Systemic Cotinine Levels in Blood, Urine and Saliva”.

For this we require patients, both smokers and non-smokers. If you agree to take part, you will be asked some questions about your contact with cigarette smoke and requested to provide two saliva samples and some scrapings from your cheek,- this procedure will be performed painlessly. In addition, we will also require a sample of urine and blood. You may already need some blood to be taken for routine examination today, and in this case, a small amount extra will be taken.

Each of these samples will take only a few minutes to collect. They will then be sent to a laboratory, and the level of nicotine compounds measured. Patient confidentiality with regard to this study is assured.

If you have any questions about this study or require further details, please contact one of the principal investigators:

Mrs V. Binnie telephone number: 0141-211-9688

Dr J Gibson telephone number: 0141-211-9833

Dr L. Macpherson telephone number: 0141-211-9751

In addition the staff and students conducting this study will be able to answer any queries.

Consent Form

I _____

of _____

freely and voluntarily agree to participate in a clinical study entitled:

The Validation of Self-Reported Smoking Status by Analysing Systemic Cotinine Levels in Blood, Urine and Saliva

I have read the accompanying information sheet. The nature and purpose of the study have been explained to me by

Dr _____

I have had the opportunity to ask questions and I fully understand what is proposed.

I recognise that I may receive no benefit from the study. I accept that there may be other risks procedure which are not directly attributable to negligence on the part of those undertaking the procedures.

I understand that I am free to withdraw my consent at any time without prejudice to me or my medical and dental care.

I have been assured that any information obtained from me will not be disclosed without my permission to any third party in a manner which will reveal my identity.

Signature _____

Date: _____

I confirm that I, Dr _____ have explained the nature and purpose of the clinical research study and the procedures in respect on which consent has been given by the above named.

Signature _____

Date _____

Appendix 4

SMOKING QUESTIONNAIRE

Name: _____

Age: yrs

Gender: Male ☐ Female ☐

Occupation: _____

Post Code:

Do you smoke cigarettes? Yes ☐ No ☐

Smokers

What do you smoke? Cigarettes ☐
Cigars ☐
Pipe ☐

How many cigarettes do you smoke per day? <10 ☐
10-20 ☐
>20 ☐

What brand of cigarettes do you smoke? _____

What is the tar level of the cigarettes you smoke? High ☐
Middle ☐
Low to Middle ☐
Low ☐
Varied ☐

Do you inhale the smoke? Not at all ☐
Slightly ☐
Medium ☐
Deeply ☐

How many hours since your last cigarette? hrs

Are you using any nicotine replacement therapy? Yes ☐ No ☐

If yes, are you using nicotine: Patches ☐
Gum ☐
Inhaler ☐

Non-Smokers

Does anyone in your household smoke around you? Yes ☐ No ☐

Does anyone in your work place smoke around you? Yes ☐ No ☐

How many hours of passive smoking have you been exposed to per day in the last week? hrs

Have you been exposed to any passive smoking during the past 24 hours?

None ☐ <1 hour ☐ 1-5 hours ☐ >5 hours ☐

Are you using any nicotine replacement therapy? Yes ☐ No ☐

If yes, are you using nicotine: Patches ☐
Gum ☐
Inhaler ☐

Time of Data Collection: _____

Patient Acceptability Questionnaire

How acceptable did you find the collection of the different samples?

Sample	Very Acceptable	Moderately Acceptable	Tolerable	Not at all Acceptable
Saliva drool	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Saliva-cotton roll	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Blood	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Urine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Appendix 5

Training of Staff Hygienists involved in the Intervention

<p><i>Basic Smoking Cessation Training</i></p> <ul style="list-style-type: none"> ▪ Two 3-hour sessions ▪ delivered by Ms Fiona Campbell, <i>Smoking Concerns</i> 	<ul style="list-style-type: none"> • Basic epidemiology of nicotine addiction and diseases caused with regards to smoking • Role of nicotine and nicotine dependence • Basic smoking cessation skills including how to give 'brief advice' • Assessing a client's readiness to change including 'Cycle of Change' • Discussing ways of motivating a quit attempt. Information on how to support a client's quit attempt • Information about resources available such as carbon monoxide monitors
<p><i>Nicotine Replacement Therapy Training</i></p> <ul style="list-style-type: none"> ▪ One 3-hour session ▪ delivered by Ms Fiona Campbell, <i>Smoking Concerns</i> 	<ul style="list-style-type: none"> • Nicotine withdrawal • Use of nicotine replacement therapy products including cautions and side-effects • Relevant clinical guidelines on the use of NRT • Demonstration of NRT products and their usage • Use of Zyban, contraindications, cautions and side-effects (for information only)
<p><i>Smoking Cessation Trial Methodology</i></p> <ul style="list-style-type: none"> ▪ One 3-hour session ▪ delivered by Mrs V. Binnie 	<ul style="list-style-type: none"> • Additional information on the oral health aspects of tobacco use and smoking cessation • Information on trial methodology, including collection of data and use of questionnaires • '5A's methodology • Salivary cotinine sampling methodology • Use of CO monitors

Appendix 6

GLASGOW DENTAL HOSPITAL & SCHOOL

378 Sauchiehall Street, Glasgow G2 3JZ

Switchboard: 0141-211 9600

Fax: 0141-211 9800

AREA DENTAL ETHICS COMMITTEE

☎ **Direct Dial: Chairman: (0141) 211 9855**
Secretary (0141) 211 9796

DFK/JR/1502DK

Dictated: 31 January 2001
Typed : 31 January 2001

Miss V Binnie
Lecturer in Oral Health Promotion
Post Graduate Centre
9th Floor
Glasgow Dental Hospital

Dear Miss Binnie

PROTOCOL "SMOKING RELATED BEHAVIOUR CHANGE IN PERIODONTAL PATIENTS WHO ARE GIVEN 'BRIEF' SMOKING CESSATION ADVICE, DELIVERED BY DENTAL HYGIENISTS - A RANDOMISED CONTROL TRIAL"

I refer to the above Protocol which was submitted to the last Ethics Committee meeting on 15 January 2001.

This protocol is approved.

Yours sincerely



D Kinane
Chairman

Appendix 7

STOPPING SMOKING STUDY

Smoking weakens gums and, therefore, smokers have more severe gum infection than non-smokers. Patients who give up smoking during the course of their treatment are more likely to achieve healthy gums. We explain this to all our patients and recommend that they should give up smoking.

Smokers who require professional help to give up smoking will usually be able to obtain it from their doctor or pharmacist. However, we would like to know whether smokers are more likely to quit if skilled help is made available in our department during the course of their gum treatment, and we have designed a project to find out. An outline of this project is given below.

We are inviting smokers, whether or not they want to quit, to complete a questionnaire about their smoking habits and to give us a sample of saliva. Patients will then be divided into two groups:

Group 1 - Patients in group 1 will receive gum treatment without any help to stop smoking

Group 2 - Patients in group 2 will receive advice on how to stop smoking and will be offered free nicotine replacement therapy (gum or patches).

You will have an equal chance of being placed in either group. Of course, those who are placed in group 1, which is scheduled not to receive additional advice or nicotine replacement therapy can, if they wish, ask their doctor for this assistance or obtain help elsewhere. Patients in group 2 will be given advice to stop smoking by their dental hygienist. This advice will be given to all patients in group 2 even if they have no intention of giving up. All the dental hygienists have been specially trained to do this, and the advice will be given during normal treatment visits.

In a few months, patients in both groups will be asked for a further sample of saliva and asked whether their smoking habits have changed.

If, having read this information, you decide that you do not wish to be part of this study, please be reassured that you can decline without prejudice to your dental care. All information that you provide will be totally confidential. If you require any information about this study, please contact one of the individuals below:

Mrs V Binnie - Glasgow Dental School, tel: 0141-211-9802

Dr W Jenkins - Glasgow Dental Hospital, tel: 0141-211-9857

/

Consent Form

I _____
of _____

freely and voluntarily agree to participate in a clinical study entitled:

Smoking-related Behaviour Change in Periodontal Patients who are given 'Brief' Smoking Cessation Advice/ NRT, delivered by Dental Hygienists- a randomised control trial.

I have read the accompanying information sheet. The nature and purpose of the study have been explained to me by

I have had the opportunity to ask questions and I fully understand what is proposed.

I recognise that I may receive no benefit from the study.

I understand that I am free to withdraw my consent at any time.

I have been assured that any information obtained from me will not be disclosed without my permission to any third party in a manner which will reveal my identity.

Signature _____

Date: _____

I confirm that I, _____ have explained the nature and purpose of the clinical research study and the procedures in respect on which consent has been given by the above named.

Signature _____ Date _____

Glasgow Dental Hospital & School

Appendix 8

GDH number

Study number

Hygienist Initials _____ Date _____

SMOKING QUESTIONNAIRE - BASELINE

Name: _____

Age: yrs

Gender: Male ☐ Female ☐

Occupation: _____

Post Code:

Please Tick

✓

How many cigarettes do you smoke per day?	10 or less	<input type="checkbox"/>
	11-20	<input type="checkbox"/>
	21-30	<input type="checkbox"/>
	31 or more	<input type="checkbox"/>

Can you give us an exact number per day ☐☐

How soon after you wake up do you smoke your first cigarette?	Within 5 minutes	<input type="checkbox"/>
	6-30 minutes	<input type="checkbox"/>
	31-60 minutes	<input type="checkbox"/>
	Longer than that	<input type="checkbox"/>

Which cigarette would you hate most to give up?	First in the morning	<input type="checkbox"/>
	Any of the others	<input type="checkbox"/>

Do you smoke more frequently during the first hours after waking than during the rest of the day?	YES	<input type="checkbox"/>
	NO	<input type="checkbox"/>

Do you smoke when you are so ill that you spend most of the day in bed?	YES	<input type="checkbox"/>
	NO	<input type="checkbox"/>

Do you find it difficult to refrain from smoking in public places where it was forbidden eg cinema, on airplanes, public buildings etc?	YES	<input type="checkbox"/>
	NO	<input type="checkbox"/>

How many years have you smoked ? _____

What brand of cigarettes do you smoke? _____

What tar level? _____

How often do you inhale the smoke?

Please tick ✓

Never

☐

Sometimes

☐

Always

☐

Does anyone in your household smoke around you?

YES

☐

NO

☐

Does anyone in your work place smoke around you?

YES

☐

NO

☐

Would you give up smoking altogether, if you could do so easily?

Yes, definitely

☐

Yes, probably

☐

Possibly

☐

Probably not

☐

Definitely not

☐

How much do you want to stop altogether?

Not at all

☐

Slightly

☐

Moderately

☐

Quite strongly

☐

Very strongly

☐

If you want to stop, what are your main reasons? (Please tick ✓ ALL that apply)

Your health

YES ☐

NO ☐

The expense

YES ☐

NO ☐

Not fair on other people

YES ☐

NO ☐

Don't like being addicted

YES ☐

NO ☐

Some other reason

YES ☐

NO ☐

What do you think your biggest problem will be in stopping smoking?

And finally, which of the three statements below best describes you?
Please tick ✓ only ONE.

	YES
Are you a smoker at the moment and not thinking about giving up?	<input type="checkbox"/>
Are you concerned about your smoking and thinking about giving up in the next 6 months?	<input type="checkbox"/>
Are you ready to stop smoking and are thinking about giving up in the next 30 days?	<input type="checkbox"/>

And about your quit attempts in the last year?

	YES	NO
Have you tried quitting in the last year?	<input type="checkbox"/>	<input type="checkbox"/>
If you answered YES to the above question, Could you answer the two questions below.		
Have you had two or more quit attempts?	<input type="checkbox"/>	<input type="checkbox"/>
Had a quit attempt lasting a week or more?	<input type="checkbox"/>	<input type="checkbox"/>

Thank you for your help in answering this questionnaire.

Carbon Monoxide Level ☐ ☐

Cotinine sample ☐ Time of sample _____ Time of last cigarette _____

Appendix 9

Smoking Cessation 5As Protocol

Study Number

Case Number

Visit number Date _____

Patient Name _____

ASK (can refer to questionnaire)

Smoking History

- How long has patient smoked?
- How many at present?
- Patient smoke regularly throughout day or mainly evening?
- What products are used? _____

ADVISE

- Advice to be clear, strong and personalised.
- **'I believe that it is important for you to quit smoking for your oral health as well as your general health and we can help you.....'**
- emphasise the perio aspect of smoking as well as oral cancer.

ASSESS

willingness to quit

- patient willing to make a quit attempt _____ **ASSIST**
- patient unwilling to make a quit attempt _____ **5R's**
- patient willing to make some change in smoking behaviour
(Risk Reduction)

ASSIST

- **SET QUIT DATE** (ideally within 2 weeks)
- tell family and friends about quitting
- identify likely problems and solutions,

- e.g. other smokers, use of alcohol ☐
- plan how to cope with increase in food and drink ☐
- information about NRT ☐
- prescribe NRT? See NRT sheet ☐
- Information about Zyban ☐
- Give quit pack ☐
- Telephone help line number ☐

5 Rs

- Emphasise the **relevant** benefits for the patient ☐
- Emphasise the **risks** of continuing to smoke ☐
- list the **rewards** from stopping ☐
- discuss the **roadblocks** to quitting (withdrawal symptoms, lack of support) ☐
- emphasise that **repeat** attempts are more successful ☐

Risk Reduction

- thinking about reducing number of cigarettes ☐
- reduce cigarettes to less than half of consumption ☐
- Thinking about making a quit attempt of 24 hours or more. ☐

Arrange Follow –up

- Arrange next appointment ☐
- At next visit reinforce the 5 A's. ☐

Comments

CO level

Prescription for NRT

Nicotine Patches (high, 15mg) ☐

No of packs ☐

Nicotine Patches (med, 10 mg) ☐

No of packs ☐

Nicotine Patches (low, 5mg) ☐

No of packs ☐

Nicotine Gum (high) – 4mg ☐

No of packs ☐

Nicotine Gum (low) – 2mg ☐

No of packs ☐

Appendix 10

Case Record ☐☐☐☐☐☐☐

Date _____ 3 6

Study number ☐☐☐

FOLLOW-UP SMOKING QUESTIONNAIRE

Name:

Age:

Gender. Male ☐ Female ☐

Occupation: _____

Post Code: ☐☐☐☐ ☐☐☐

Please tick where required

Are you currently a **smoker** ☐ ----- - please go to **section 2 (page 2)**

Are you currently **not smoking** ☐ ----- please answer **section 1**

Section 1- Ex-Smokers

If you are an ex-smoker, when did you give up? _____

Did you use any Nicotine Replacement Therapy (gum/patches) ? YES ☐ NO ☐

If yes, what did you use?

Did you use Zyban? YES ☐ NO ☐

If YES, for how long?

What else helped you?

Section 2 - Smokers

Have you made any changes in smoking habit, if you are still smoking:

Have you made any quit attempts in the last 3 months YES ☐ NO ☐

Have you had two or more quit attempts? YES ☐ NO ☐

Have you had a quit attempt of 24 hours or longer? YES ☐ NO ☐

Have you had a quit attempt of one week or longer? YES ☐ NO ☐

Have you managed to delay smoking for longer than
five minutes after waking YES ☐ NO ☐

Have you managed to reduce smoking:

Reduce number of cigarettes YES ☐ NO ☐

If YES. can you tell us from _____ cigarettes to _____ cigarettes.

Inhale Less YES ☐ NO ☐

Smoke less of a cigarette before stubbing out
 YES ☐ NO ☐

Changed to a low-tar brand YES ☐ NO ☐

Any other changes in smoking habits:

How many cigarettes do you smoke per day?	10 or less	<input type="checkbox"/>
	11-20	<input type="checkbox"/>
	21-30	<input type="checkbox"/>
	31 or more	<input type="checkbox"/>

Can you give us the exact daily number ☐☐

How soon after you wake up do you smoke your first cigarette?

- Within 5 minutes ☐
- 6-30 minutes ☐
- 31-60 minutes ☐
- Longer than that ☐

Which cigarette would you hate most to give up?

- First in the morning ☐
- Any if the others ☐

Do you smoke more frequently during the first hours after waking than during the rest of the day?

- YES ☐
- NO ☐

Do you smoke when you are so ill that you spend most of the day in bed?

- YES ☐
- NO ☐

How many years have you smoked ?

What brand of cigarettes do you smoke?

What tar level?

Do you inhale the smoke?

Please tick

- Never ☐
- Sometimes ☐
- Always ☐

Does anyone in your household smoke around you? YES ☐ NO ☐

Does anyone in your work place smoke around you? YES ☐ NO ☐

Would you give up smoking altogether, if you could do so easily?

Yes, definitely

☐

Yes, probably

☐

Possibly

☐

Probably not

☐

Definitely not

☐

How much do you want to stop altogether?

Not at all

☐

Slightly

☐

Moderately

☐

Quite strongly

☐

Very strongly

☐

And finally, which of the three statements below best describes you?

Please tick only **ONE**.

Are you a smoker at the moment and not thinking about giving up?

YES

☐

Are you concerned about your smoking and are thinking about giving up in the next 6 months?

☐

Are you ready to stop smoking and are thinking about giving up in the next 30 days?

☐

Did you find the advice on stopping smoking from the dental staff helpful?

YES ☐

NO ☐

Any further comments regarding any aspects of this study?

Thank you for answering this questionnaire.

CO Level ☐☐

Cotinine

☐

Time taken _____

Time of last Cigarette _____

1/1

Appendix 11

1 year Telephone Reviews in Smoking Cessation Trial

Name _____

Log number ☐ ☐ ☐

Allocation I C

Hygienist EW VG PJ

Date of Baseline Questionnaire. ☐ ☐ ☐ ☐ ☐ ☐

Have you smoked a cigarette, even a puff, in the past 7 days?

YES ☐ NO ☐

If yes, do you consider yourself to be a regular smoker YES ☐ NO ☐

If yes, how many cigarettes per day? ☐ ☐

If no, describe your smoking habits

If you are a smoker, or have started smoking again, have you tried any further quit attempts, or feel more able to try a further quit attempt.

YES ☐ NO ☐

Why do you think you smoke the same or more than you did a year ago?

(DO NOT PROMPT) ☐

Wasn't ready to give up ☐

Related to stress ☐

Patches didn't work ☐

Too hard to give up ☐

Changed my mind ☐

Individual problems/circumstances ☐

Other (please specify)

Total Cessation/Occasional smoker/regular smoker/unreported

Occasional – less than 5 cigarettes per week.

/

Log number

Please fill in the questionnaire below

1. Have you smoked a cigarette, or even a puff in the past 7 days?

Yes ☐

No ☐

2. If yes, do you consider yourself to be a regular smoker?

Yes ☐

No ☐

3. If yes, how many cigarettes per day?

4. If no, please describe your smoking habits

5. If you are a smoker, or have started smoking again, have you tried any further quit attempts, or feel more able to try a further quit attempt.

Yes ☐

No ☐

6. Why do you think you still smoke?

Thank You for taking the time to complete this questionnaire

Appendix 12

Rates of abstinence for six months or longer compared with will-power or placebo alone

Intervention	Effect size
Written self-help materials	1%
Telephone counselling	2%
Brief opportunistic advice from a GP or outpatient doctor to stop	2%
Face to face intensive behavioural support from a specialist	4-7%
Various forms of NRT with limited or intensive behavioural support	5-12%
Bupropion (300 mg/day sustained release) with intensive behavioural support	9%

Adapted from *Smoking Cessation Guidelines for Health Professionals: an update* (West *et al.*, 2000). The effect size is the difference in >6 month abstinence rate between intervention and control/placebo in the studies. Studies were mainly Cochrane meta-analyses.

Appendix 13

Lancaster BSDR Meeting, 2000

Passive smoking and it's effects on cotinine levels

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Cotinine can be used to quantify exposure to environmental tobacco smoke (passive smoking). The aim of this study was to examine reported levels of nicotine exposure due to passive smoking and relate this to the levels of cotinine found in different body fluids. 33 non-smokers participated, with each being asked to provide samples of blood, urine and both stimulated and unstimulated saliva, together with information on their environmental exposure to smoke either in the home or workplace. 33% of participants were exposed to smoke at home and 18% were exposed to smoke in the workplace. In the 24 hours prior to providing the fluid samples, 64% of participants had no exposure to smoke and 36% had been exposed to smoke. The mean cotinine levels of serum, urine (corrected for concentration using the cotinine/creatinine ratio), stimulated and unstimulated saliva in participants with no exposure to smoke in the previous 24 hours were 3.1, 1.8 1.4 and 0.4 ng/ml, respectively, whilst the mean cotinine levels in non-smokers who had been exposed to smoke were 34.0, 10.8, 12.5 and 7.6 ng/ml respectively. However, due to the relatively small number of participants, no statistical significant difference was found between the mean cotinine levels of non-smokers who were and were not exposed to smoke, for each of the four types of sample (all p-values >0.05).

This study suggests that there may be a difference in the cotinine levels of non-smokers who have and have not been exposed to smoke and further work with a larger sample is indicated.

Lancaster BSDR Meeting, 2000

The effect of nicotine exposure on the cotinine levels in smokers

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University of Glasgow, Scotland, ¹Glasgow Royal Infirmary

Determination of a smoker's degree of exposure to nicotine, can be assessed by measuring the level of cotinine in various biological fluids. The aim of this study was to relate reported smoking habits to the levels of cotinine found in a group of smokers. Participants were asked about the number of cigarettes smoked per day, tar level and inhalational habits. A total of 52 smokers took part (24 males). The participants were asked to contribute four different biological samples: blood, urine and samples of both stimulated and unstimulated saliva. With regards to the serum levels, those smoking <10 cigarettes a day had a mean cotinine level of 261 ng/ml, which was significantly lower than the mean cotinine level of 395 ng/ml for those smoking >20 cigarettes/day ($p=0.04$). The mean cotinine level measured from the urine samples was 142 ng/ml for participants smoking <10 cigarettes a day. This was significantly lower than both the mean cotinine level of those smoking 10-20 cigarettes/day (357 ng/ml) and those smoking >20 cigarettes/day (522 ng/ml) ($p<0.01$). Similar patterns were found from both the saliva samples, with the mean levels of cotinine found in the stimulated sample (chewing on a cotton wool roll) being significantly lower than those found in the unstimulated (drool) sample ($p<0.01$). There was little relationship found between either the tar level and cotinine levels or the inhalational habits and the cotinine levels, in the four fluids from the smokers.

This study reveals that a dose-response can be elicited for smoking habits and this is consistent in all four biological fluids. Levels of cotinine in saliva are dependent upon the method of salivary collection used, with a significantly higher level of cotinine being found in unstimulated saliva.

Lancaster BSDR Meeting, 2000

Cotinine estimation in biological fluids – patient acceptability

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Cotinine, a metabolite of nicotine, can be used for determining exposure to nicotine via various biological fluids. In this study, participants were recruited via a dental hospital Oral Medicine department. They were asked to provide four biological samples: saliva collected via chewing on a cotton wool roll, a sample of unstimulated saliva as well as blood and urine specimens. The subjects were also asked about the acceptability of the differing methods of sample collection. Samples were analysed using an immunoassay kit (Cozart). Data were collected from 85 subjects: 52 smokers and 33 non-smokers. Using a cut-off point of 20ng/ml, correct classification of smoking status was achieved for 98%, 96%, 96% and 94% of the smokers, and 94%, 97%, 94% and 94% for the non-smokers, using the cotinine measurements from serum, urine, stimulated and unstimulated saliva, respectively. There was a significant difference between the percentages of participants who found each of the four methods 'very acceptable' ($p < 0.01$), with 67% and 65%, respectively rating the blood and urine collection methods as being very acceptable, whilst only 49% and 45% (respectively) rated the unstimulated and stimulated saliva very acceptable. 8% of participants rated stimulated saliva as 'not acceptable' (1% thought unstimulated saliva was not acceptable, whilst none of the participants found the blood or urine collection methods 'not acceptable').

This study reveals that cotinine levels, as determined by an immunoassay kit, are a good indicator of a subject's smoking status, but while cotinine estimation using saliva is often the method of choice, being a non-invasive technique, this may not be the method which is most acceptable to the patient.

Cardiff PEF Meeting 2002

Nicotine dependence and cotinine & carbon monoxide levels in smokers

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There is increasing recognition of the role that dental health professionals including hygienists can play in promoting smoking cessation. Baseline characteristics were examined in 86 smokers recruited to a smoking cessation trial in a periodontal clinic. Participants were asked to complete a questionnaire examining smoking habits and readiness to quit. Patients were also asked to provide a salivary sample for cotinine (COT) analysis and an exhaled air sample for carbon monoxide (CO) analysis, to determine baseline exposure to nicotine. The mean age of the participants was 41yrs, with 69% (59) being female. The majority smoked between 11 and 20 cigarettes with a mean of 19 cig/day. When assessing nicotine dependence the mean Heaviness of Smoking (HSI) was 3.3, with the mean Fagerstrom Test for Nicotine Dependence (FTND) being 4.8. Of the participants, 15% (13) were not interested in stopping smoking, 44% (38) were concerned about their smoking, and 40% (35) were interested in trying to stop within the next month. The mean level of CO for the participants was 22ppm, and the mean level of COT was 244ng/ml. There was a statistically significant positive correlation of 0.51 between CO and COT levels. The mean COT for the highly dependent group (FTND ≥ 6 , n=34) was 281ng/ml, which was significantly higher than that of the less dependent group (FTND < 6, n=52, mean COT 220ng/ml). A similar relationship was also found between CO levels in the two dependency groups (27ppm and 18ppm, respectively).

Significant associations between COT and CO were found in relation to the level of dependency as measured by FTND; this may be an important predictor of likelihood of quitting.

Dental Hygienists' Delivery of Smoking Cessation: 3-month Outcomes

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Objectives: To examine the feasibility and efficacy of a smoking cessation intervention, delivered by dental hygienists, in a cohort of patients attending a specialist periodontal department in a dental hospital.

Methods: One hundred and eighteen new patients were recruited into a randomised controlled smoking cessation trial. Dental hygienists offered those patients allocated to the intervention group smoking cessation advice based on the 5As and free nicotine replacement therapy, in addition to their periodontal treatment. The patients in the control group were only given brief advice at point of recruitment. At baseline, all participants were asked to complete questionnaires assessing their smoking habits and readiness to quit, as well as providing a salivary sample for cotinine analysis. Follow-up information and questionnaires were available for 103 (87%) of the participants at 3 months.

Results: The mean age of the participants was 41 years (SD 10), with 70% being female. In the intervention group, 17% of the participants quit, compared with 12% of the control group (biochemically validated). With regards to secondary outcomes in smokers, a significantly greater percentage of participants in the intervention group claimed to have reduced their smoking than in the control group (79% vs 47%, $p=0.002$). There was a significantly higher mean percentage reduction in cigarettes per day in the intervention group (32%) than in the control group (19%) ($p=0.013$, 95%CI (3, 23)%). When asked about their quit attempts, 36% of the intervention group claimed to have had a quit attempt of 1 week or more, compared with 18% of the control group ($p=0.059$).

Conclusion: There is increasing recognition of the role that dental health professionals including hygienists can play in promoting smoking cessation. Dental hygienists in a hospital setting can deliver effective smoking cessation advice as part of their contribution to treatment.

Prediction of Primary and Secondary Outcomes in a Smoking Cessation Trial

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Objective: To identify significant factors in predicting changes in smoking behaviour of participants in a smoking cessation trial.

Methods: One hundred and eighteen participants were recruited into a randomised controlled trial which aimed to compare the delivery of smoking cessation advice and nicotine replacement therapy, delivered by dental hygienists, with brief advice alone given at the recruitment visit. Participants completed questionnaires at baseline eliciting smoking habits and readiness to quit. Potential predictors extracted from the baseline data included demographics, smoking habits, level of physiological dependency on nicotine, as defined by the Fagerstrom Test for Nicotine Dependence (FTND) and the Heaviness of Smoking Index (HSI), motivation and intention to quit (Cycle of Change), together with the allocated group. After 3 months, the primary outcome of smoking status and the secondary outcomes of quit attempt of ³1 week and reduction in number of cigarettes smoked were examined (data available for 103 participants). Classification trees were used to identify significant factors in predicting both primary and secondary outcomes.

Results: In predicting the primary outcome of quitting smoking at 3 months, a combination of low HSI and preparing to quit (Stage 3 of Cycle of Change) at baseline identified the only subgroup of participants predicted to quit smoking. However, this model only correctly identified 6/15 quitters. More successful models were obtained for predicting secondary outcomes, with both models having sensitivity of approximately 75% and specificity of approximately 85%. The allocated group was a significant factor in predicting both secondary outcomes, as were the measures of nicotine dependence, smoking habits and motivation at baseline.

Conclusion: Classification trees can be used to produce informative models in predicting 3 month outcomes of a smoking cessation trial; these were most efficient with regard to the secondary outcomes.

Clinical Biochemistry

The validation of self-reported smoking status by analysing cotinine levels in stimulated and unstimulated saliva, serum and urine

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OBJECTIVES: Cotinine, a nicotine metabolite, can be used to measure exposure to tobacco smoke. The aim of this study was to compare cotinine levels in different biological fluids collected from both smokers and non-smokers and to relate the findings to self-reported smoking status. Data were also collected concerning the acceptability of the differing methods of sample collection.

MATERIAL AND METHOD: Patients recruited to the study were asked to provide samples of urine, blood and saliva (both stimulated and unstimulated). Data collected from patients by questionnaire included information on smoking behaviour such as daily number of cigarettes and environmental exposure to smoke. After the sample collection, patients were asked to rate the acceptability of each sampling method. Samples were analysed using enzyme immunoassay (EIA) kits.

RESULTS: In total, 80 patients participated, with 49 being smokers and 31 being non-smokers. There was clear differentiation between smokers and non-smokers ($P < 0.001$) for all the different samples in terms of cotinine. A significant relationship was seen between cotinine and daily number of cigarettes for both salivas and urine (all $P < 0.001$) but not for serum. Participants found serum and urine collection methodologies 'very acceptable' (67 and 66%, respectively) whereas 9% found collection of stimulated saliva 'not at all acceptable'.

CONCLUSION: Cotinine, whatever the collection method and analysed by EIA kits, shows good differentiation between smokers and non-smokers. Salivary samples have the advantage of being non-invasive, although collection methodology is important, as cotinine levels may vary.

Oral Diseases (2004) 10, 287–293

Keywords: tobacco; cotinine; cross-sectional study

Introduction

Tobacco use is the single biggest contributor to ill health, and is the most important preventable cause of death in the UK (Callum, 1998). There is growing awareness and interest in the role that dental health professionals can play in helping their patients quit the tobacco habit, whether in secondary or primary care (Chestnutt and Binnie, 1995; McCann *et al*, 2000; Warnakulasuriya 2002; Watt and Daly, 2003).

In addition to being implicated in coronary health disease, lung and other cancers, smoking also has a profound effect on the oral tissues. Cigarette smoking is associated with increased prevalence and severity of periodontitis and smokers suffer from more tooth loss (Krall *et al*, 1997; Tonetti, 1998). In addition, the risk of oral cancer and potentially malignant lesions is higher amongst smokers compared with those who have never smoked. Patients who smoke have a sixfold increased risk of developing oral leukoplakia compared with non-smokers (Baric *et al*, 1982). There is some evidence that if patients with such lesions can be encouraged to quit the tobacco habit, such lesions will regress (Gupta *et al*, 1986; Chad Martin *et al*, 1999). However, neither of these studies used biochemical validation to monitor changes in tobacco exposure.

When evaluating the effectiveness of tobacco cessation advice, it is important that some form of biochemical validation is used. The most commonly used means of evaluating tobacco exposure is the measurement of carbon monoxide in an exhaled air sample. Although advantages of this method include cost and ease of use, disadvantages include non-specificity and a short half-life of 3–6 h, which can lead to false negatives. One biochemical marker that is able to determine exposure to tobacco smoke over a longer timeframe, with a half-life of 20 h, is cotinine. This compound is a metabolite of nicotine and can be measured in a number of

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biological fluids including blood, saliva, cervical exudate, semen and urine (Etzel, 1990; Vine *et al*, 1993; Poppe *et al*, 1995). Cotinine is sufficiently sensitive to be detected also in the body fluids of those individuals exposed to passive or environmental tobacco smoke (Cummings *et al*, 1990).

Most studies using cotinine assays have relied on serum samples, which can be problematic in field settings. Urine is non-invasive to collect, but requires access to facilities for its collection.

Salivary samples, taken for use in cotinine analysis, also have the benefit of being non-invasive, and have been shown to be stable if sent by post, thus enabling their use in outreach studies (Greeley *et al*, 1992; Smith *et al*, 1998). Salivary cotinine has also been used extensively to determine exposure to smoke in large population studies, such as the health surveys in Scotland and England (Shaw *et al*, 2000; Bajekal *et al*, 2003).

Most previous studies using saliva have failed to specify exactly how the saliva is collected although it has been suggested that levels of cotinine can vary depending on whether the saliva collected is stimulated or unstimulated. However, one study has examined the relationship between cotinine levels and collection method and found that stimulated samples had lower levels of cotinine than those found in unstimulated saliva (Schneider *et al*, 1997).

Traditionally, cotinine has been measured using a number of techniques including radioimmunoassay, gas liquid chromatography or liquid chromatography (Feyerabend and Russell, 1990). However, more recently, a microplate enzyme immunoassay (EIA) has become available in the UK. An advantage of these kits is that large, expensive equipment is not required, but to date the kits are relatively unevaluated in the UK.

With regards to the patient's perspective, no published work has previously investigated patient acceptability of the different sampling methods used to collect biological samples for cotinine analyses.

The main aim of this study was to measure and compare cotinine levels using the microplate EIA technique in a variety of biological fluids, collected from a group of patients, both smokers and non-smokers, recruited in an outpatient oral medicine department. Further aims were to:

- (a) Correlate self-reported smoking exposure data with the biochemical determination of cotinine levels in the various body fluids;
- (b) Compare the patient acceptability of the differing methods of sample collection.

Material and method

Following approval from the Greater Glasgow Area Dental Ethics Committee, recruitment was via patients attending the oral medicine outpatient clinic at Glasgow Dental Hospital and School. Initially, smokers were invited to participate and non-smokers were then recruited, in an attempt to match age and gender to the case group. Data were collected over a 3-month

period in early summer, by two student researchers and one academic researcher. A convenience sample was used, with as many patients recruited as possible within the available timeframe.

The age range for the participants was 16–75 years. Exclusion criteria included medical conditions such as an incipient diagnosis of oral carcinoma or medication affecting salivary function. For smokers, only those who used cigarettes were included in the study: those individuals who smoked a pipe or used cigars were excluded, as were any individuals currently using nicotine replacement therapy.

Participating patients were asked to fill in a questionnaire about their tobacco smoke exposure. The questionnaire sought information on daily number of cigarettes smoked, time of first cigarette of the day, inhalational habits and brand and tar levels of current cigarettes used. The time elapsed since the most recent smoking occasion was also noted.

For non-smokers, information on exposure to tobacco smoke both at home and in the workplace was collected. Additionally, details relating to tobacco smoke exposure in the last 24 h was recorded.

Samples were then collected from each patient in the following order:

1. An unstimulated sample of saliva was collected by asking the patient to drool into a universal container (minimum volume = 3 ml).
2. A sample of stimulated saliva was collected by asking the patient to chew the cotton wool roll from a Salivette collection device (Sarstedt Aktiengesellschaft & Co., Numbrecht, Germany). When saturated, this was removed from the mouth and placed into the salivette.
3. A sample of blood (5 ml) was collected in a plain container using standard venepuncture techniques.
4. A sample of urine (25 ml) was collected in a plain universal container.

Patients were then asked to fill in a short questionnaire concerning the acceptability of the four different methods of sample collection. A four-point Likert scale was used which asked the respondents to rate the sample collection from 'completely unacceptable' to 'completely acceptable'.

Blood samples were stored in a fridge overnight, to allow clotting before the serum was separated and stored at -20°C . Stimulated saliva samples collected using the Salivette devices were centrifuged at 1200 *g* for 10 min. The supernatant was then removed and stored at -20°C . The unstimulated saliva and urine samples were stored at -20°C . On the day of analysis, the unstimulated saliva was thawed and centrifuged and the supernatant transferred to inert plastic tubes.

Cotinine concentrations were measured using a microplate EIA (Cozart Biosciences Ltd, Abingdon, UK). Different versions of the assay, with appropriate standards, are available for each of the three biological matrices. Quality control material was prepared by spiking cotinine-free serum, urine and saliva with cotinine standard (Sigma Chemicals) to give two levels, low

and high within each standard range for each matrix. Where required, dilutions of the patients' samples were made using cotinine-free serum, urine and in the case of saliva, deionized water. Serum and salivary cotinine concentrations are expressed as ng ml⁻¹. Urine creatinine was measured by the Olympus kinetic Jaffe reaction on an Olympus 640 analyser (Olympus UK Ltd, Southall, UK). To take account of urine dilution, all urine cotinine results were expressed as a ratio (ng mmol⁻¹ creatinine).

A cut-off of 15 ng ml⁻¹ of cotinine was used to differentiate smokers from non-smokers in serum and saliva, whilst for the urine sample analysis, a cut-off of 50 ng mmol⁻¹ of cotinine was used to determine smokers (SRNT Subcommittee on Biochemical Verification, 2002).

Statistical analysis

For smokers and non-smokers separately, the cotinine levels were approximately normally distributed. When comparing smokers and non-smokers, it was necessary to logarithmically transform the data, due to greatly differing variances in the cotinine levels. Subsequent analysis was performed on the transformed data and reported confidence intervals to compare smokers and non-smokers are for the ratios of the geometric means. Similar analysis was required when comparing non-smokers who were exposed/not exposed to smoke.

For smokers and non-smokers separately, a repeated measures analysis of variance was used to determine whether there were any significant differences between the four collection methods in terms of mean cotinine levels. Subsequent follow-up multiple comparisons were carried out to identify which methods differed significantly. Generalized linear models were used to identify which self-reported factors, for smokers and non-smokers separately, had a significant effect on the cotinine levels, again with suitable follow-up multiple comparisons where necessary.

Results

In total, 80 patients were recruited. Of the participants, 49 (25 male, 24 female) were smokers (61%) and 31 (15 male, 16 female) were non-smokers (39%). The mean age of the smokers was 44 years (s.d. 18 years) and for the non-smokers 47 years (s.d. 17 years). Thirty-eight (48%) of the participants were from relatively affluent backgrounds, i.e. residing in DEPCAT 1-4 areas (21 smokers and 17 non-smokers).

Comparison of smokers vs non-smokers

The mean cotinine level for the four fluids, for smokers and non-smokers separately, is shown in Table 1, together with the 95% confidence interval for the ratio of the geometric mean cotinine levels (smokers/non-smokers). Corresponding *P*-values from the two-sample *t*-tests of equal mean levels of cotinine in smokers and non-smokers are also given.

A clear differentiation between the smokers and non-smokers was seen (with *P* < 0.001 for all fluids) with confidence intervals illustrating the much greater mean

Table 1 Mean levels of cotinine for smokers and non-smokers for each sampling method

	Smokers (<i>n</i> = 49), mean (s.d.)	Non-smokers (<i>n</i> = 31), mean (s.d.)	95% CI ^a (smokers/ non-smokers)	<i>P</i> -value
Serum (ng ml ⁻¹)	328.4 (207.5)	3.6 (2.8)	59.7 111.7	<0.001
Stimulated saliva (ng ml ⁻¹)	194.3 (122.5)	2.0 (0.9)	28.5 105.4	<0.001
Unstimulated saliva (ng ml ⁻¹)	314.0 (171.9)	1.6 (1.2)	120.8 235.5	<0.001
Urine (ng mmol ⁻¹)	302.5 (244.0)	1.1 (1.9)	224.9 776.3	<0.001

^aCI is for ratio of geometric mean of smokers to geometric mean of non-smokers.

cotinine level of smokers. The mean level of cotinine in non-smokers in all the fluids was below 10 ng ml⁻¹, whereas the mean level of cotinine in the smokers varied from 194 ng ml⁻¹ in stimulated saliva to 328 ng ml⁻¹ in serum.

Comparison of collection methods

Repeated measures ANOVA indicated that there were significant differences in the mean cotinine levels between the four collection methods, for both smokers and non-smokers (both *P* < 0.001). Subsequent multiple comparisons indicated that for smokers the cotinine levels in serum, urine and unstimulated saliva were significantly greater on average than the levels found in stimulated saliva (Table 2). For non-smokers, where cotinine is being measured in very small amounts, there were significant differences between the serum and all other types of sample, with the mean serum level being significantly higher. When comparing the urine and stimulated saliva in non-smokers, the mean level in the stimulated saliva was significantly higher. This last finding is the opposite relationship to that found with these two samples in smokers, where the mean level of cotinine in urine is higher than that found in the stimulated saliva.

Relationships between self-reported data and cotinine levels for smokers

Results from generalized linear models, incorporating number of cigarettes smoked per day (<10, 10-20 or

Table 2 Multiple comparisons of sampling methods for smokers and non-smokers

	95% Simultaneous CI for difference in average cotinine levels	
Fluid-fluid	Smokers (<i>n</i> = 49)	Non-smokers (<i>n</i> = 31)
Serum-stimulated saliva	59.7-217.7	0.9-2.5
Serum-unstimulated saliva	-63.7-93.2	1.2-2.8
Serum-urine	-52.0-103.9	1.8-3.4
Urine-stimulated saliva	33.7-191.8	-1.7-0.1
Urine-unstimulated saliva	-89.7-67.3	-1.3-0.3
Unstimulated saliva- stimulated saliva	44.4-203.5	-1.2-0.4

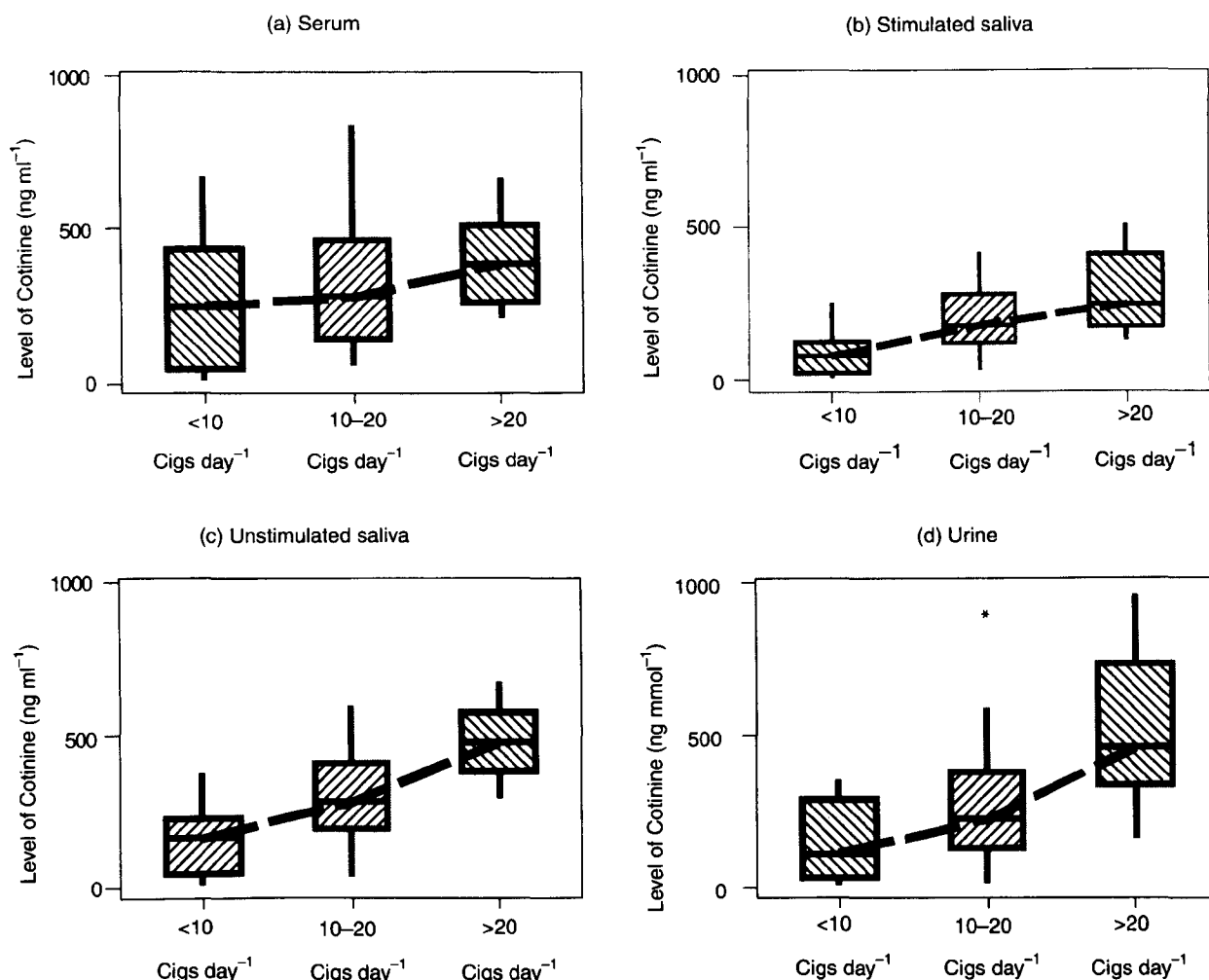


Figure 1 Boxplots of levels of cotinine by number of cigarettes smoked per day for each collection method. Boxplots illustrating dose response relationship between cotinine and number of cigarettes smoked per day (median trace of cotinine level across NOCS)

> 20), tar level of cigarettes smoked (low, medium or high) and inhalational habits (slightly, moderately or deeply) for each of the collection methods separately, suggested that the only factor having a significant influence on the smokers' cotinine levels was number of cigarettes smoked per day (NOCS). The boxplots shown in Figure 1 show a cotinine dose-response relationship with NOCS. This dose-response relationship between cotinine level and NOCS was statistically significant for stimulated saliva (Figure 1b), unstimulated saliva (Figure 1c) and urine (Figure 1d) (all $P < 0.001$) but was not statistically significant for serum ($P = 0.291$) (Figure 1a).

For stimulated saliva, the mean cotinine level for < 10 cigarettes day⁻¹ was significantly lower than that for 10–20 and > 20 cigarettes day⁻¹, but there was no significant difference between the mean cotinine level for 10–20 and that for > 20 cigarettes day⁻¹. For unstimulated saliva, there was a significant difference between each of the three categories of NOCS. For urine, there was no

significant difference between the average levels of cotinine for < 10 and 10–20 cigarettes day⁻¹, but both of these had on average lower levels of cotinine than the > 20 cigarettes day⁻¹ category.

Relationships between self-reported data and cotinine levels for non-smokers

For non-smokers, generalized linear models were used to determine which of the three factors – exposed to passive smoke at home (yes or no), at work (yes or no) and exposed to passive smoke in the previous 24 h (yes or no) – had a significant influence on the mean cotinine level, for each of the four collection methods in turn (see Table 3).

For each of the fluids, the most dominant factor was exposure to smoke at home. This factor had a significant effect on the average cotinine levels of stimulated saliva, unstimulated saliva and urine (all $P < 0.05$). For each of these fluids exposure to smoke at home significantly increased on average the mean level of cotinine,

Table 3 Mean levels of cotinine for non-smokers for each sampling method by exposure to smoke at home

	Exposed to smoke at home (n = 10), mean (s.d.)	Not exposed to smoke at home (n = 21), mean (s.d.)	95% CI ^a (exposed/not exposed)	P-value
Serum (ng ml ⁻¹)	5.4 (4.7)	2.9 (0.8)	0.4–1.4	0.25
Stimulated saliva (ng ml ⁻¹)	2.7 (1.4)	1.7 (0.4)	0.5–0.9	0.02
Unstimulated saliva (ng ml ⁻¹)	2.5 (1.9)	1.3 (0.4)	0.4–1.0	0.04
Urine (ng mmol ⁻¹)	2.3 (2.0)	0.6 (1.5)	0.1–0.5	<0.01

^aCI is for ratio of geometric mean of exposed to geometric mean of not exposed.

compared with the mean level of cotinine of participants not exposed to smoke at home.

Patient acceptability of each collection method

Figure 2 gives the percentages of patients who found each of the four collection methods 'very acceptable', 'moderately acceptable', 'tolerable' and 'not at all acceptable'. There was no difference between the patterns of acceptability of smokers and non-smokers. High numbers of patients found both serum and urine collection methodologies 'very acceptable' (67 and 66%, respectively), significantly greater than that for the stimulated saliva collection (45%). No participant rated the serum or urine collection methods as being 'not at all acceptable', whilst almost one in 10 (9%) found collection of the stimulated saliva 'not at all acceptable'. The unstimulated saliva fared better than the stimulated saliva, with 51% of the participants rating the former collection method as 'very acceptable' and only 1% 'not at all acceptable'.

Discussion

For monitoring purposes within a smoking cessation trial, usually only one type of biological sample would be collected. Choice of sample type depends upon the sampling means available and the setting in which the sample is collected.

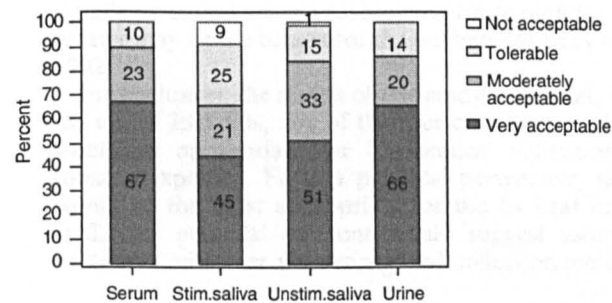


Figure 2 Barcharts of patient acceptability for each collection method. Percentage of patients finding serum, stimulated saliva, unstimulated saliva and urine collection methods 'very acceptable', 'acceptable', 'moderately acceptable', and 'not at all acceptable'

This study aimed to compare cotinine levels and patient acceptability in four different collection methods within an oral medicine setting. It is acknowledged that the utilization of a convenience sample may have resulted in participants not being necessarily representative of the typical oral medicine patient population. Although a reasonable number of participants were recruited, the matching of non-smokers and smokers was incomplete due to time constraints, resulting in an unequal number of patients in the two groups.

In this study, using the appropriate microplate EIA kit for each type of sample, good differentiation was obtained between smokers and non-smokers. Levels of cotinine varied among the different samples collected in the study. The half-life of cotinine in saliva and serum is approximately the same, and cotinine concentrations in these two matrices have previously been found to be correlated. Bernert *et al* (2000) reported that levels of cotinine in salivary samples (collected via salivette devices) were predictive of serum cotinine levels by $\pm 10\%$. However, in the present study, serum levels were found to be more closely correlated with unstimulated than stimulated saliva: for smokers the serum cotinine was on average 4 and 41% greater than the unstimulated and stimulated salivas, respectively.

In this study, the mean level of cotinine in smokers was found to be greater in the unstimulated (314 ng ml⁻¹) compared with the stimulated (194 ng ml⁻¹) saliva. These findings were consistent with those of Schneider *et al* (1997), who postulated that the reason for the difference may lie in the pH changes which alter with the flow rate. Cotinine has a pK_a close to the pH of saliva and plasma. As the pH of unstimulated saliva is less than that of stimulated saliva, a basic compound such as cotinine would be influenced by the flow. Under more acidic conditions such as those produced by unstimulated saliva, there would be higher concentrations available of cotinine. Thus, as flow rate is increased with stimulation, less of the substance would be captured for measurement.

A cotinine dose-response relationship to nicotine exposure is important as it helps to quantify the relative risk that patients are undergoing. In this study, the two salivary samples and urine samples were able to differentiate between categories of light, medium and heavy smoker, whereas serum samples were not able to exhibit this finding. Machacek and Jiang (1986) found similar findings, with poor correlation between cotinine concentrations in plasma and number of cigarettes smoked. With regards to saliva and cotinine levels, Etter *et al* (2000) found cotinine concentration to be moderately associated with the number of cigarettes per day.

Given the reported relationship between cotinine concentrations and cigarettes per day, it may be possible to use this analysis in longitudinal studies to differentiate between smokers who report they have reduced smoking but who continue to compensatory smoke by inhaling more deeply (i.e. cotinine levels will be maintained), and smokers who actually cut down smoking exposure prior to quitting totally. This is an area requiring further investigation.

Patient acceptability of the different methods of sample production provided some unexpected findings. It was postulated that patients might rate venepuncture least favourably because of the invasive nature of the technique. However, surprisingly they rated the stimulated saliva collection most negatively. Some participants found the chewing of the cotton wool roll an unpleasant sensation and, in extreme cases, felt nauseous, which may have led to a poor acceptability rating being recorded. From a participant's point of view, the unstimulated saliva appeared to be the more acceptable of the two salivary collection methods, and hence would be the choice for any future work within a dental setting. Acceptability levels associated with alternative means of stimulating saliva would require further investigation.

The high acceptability of the blood sampling methodology may be related to the setting in which this cross-sectional study took place: a dental hospital oral medicine department where venepuncture is often a routine part of investigation. It is postulated that work carried out in a different dental setting such as general dental practice or a periodontal clinical may yield differing results in terms of patient acceptability of collection methods.

It is important that any future smoking cessation interventions within a dental setting are monitored, and that quit rates are biochemically verified. One study which took place in a hospital periodontal department, found a difference in quit rates between intervention and control groups of 7%. However, this information was gathered by self-report (Macgregor, 1996). The first UK study of smoking cessation in general dental practice did use cotinine to biochemically verify those participants who reported that they had quit smoking and had a success rate of 11% (Smith et al, 1998). Whole mouth salivary samples were collected for cotinine analysis by gas chromatography.

For future smoking cessation work, baseline verification of cotinine levels, followed by cotinine assessment once smoking cessation interventions have taken place offer a good means of monitoring and evaluating the process of smoking cessation interventions as they are delivered. For patient motivation and feedback, if this is combined with a more immediate means of determining exposure, similar to that obtained with an exhaled air sample measured using a carbon monoxide monitor, the greater may be the benefit for the patients (Murray et al, 2002).

In conclusion, the results of this study show that, with the use of EIA kits, any of the four collection methods would be appropriate for biochemical validation of tobacco exposure. From a practical perspective, saliva would be the most appropriate for use by oral health staff, and patients' opinions would suggest using an unstimulated rather than stimulated collection method.

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Tobacco and Smoking Cessation.

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Tobacco-related Research Abstracts

BSDR Lancaster 2000

Passive smoking and the effect on cotinine levels

V. Binnie, S. McHugh, K. Malik, K. Moir, L. Macpherson, W. Borland¹
(University of Glasgow, Scotland, ¹Glasgow Royal Infirmary)

The effect of nicotine exposure on the cotinine levels in smokers

K. Malik, V. Binnie, K. Moir, L. Macpherson, W. Borland¹, S. McHugh
(University of Glasgow, Scotland, ¹Glasgow Royal Infirmary)

Cotinine estimation in biological fluids – patient acceptability

K. Moir, V. Binnie, K. Malik, L. Macpherson, W. Borland¹, S. McHugh
(University of Glasgow, Scotland, ¹Glasgow Royal Infirmary)

Cardiff PEF Meeting, 2002

Nicotine dependence and cotinine & carbon monoxide levels in smokers

V.I. Binnie, S. McHugh, L.M. Macpherson, W. Jenkins, W. Borland

(Glasgow Dental Hospital & School, ¹Dept of Biochemistry, Gartnavel General Hospital, Glasgow)

Gothenburg IADR Meeting, 2003

Dental Hygienists' Delivery of Smoking Cessation: 3-month Outcomes

V. Binnie¹, S. McHugh¹, L.M. Macpherson¹, W. Jenkins², W. Borland³

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Prediction of Primary and Secondary Outcomes in a Smoking Cessation Trial

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Research Grants in Smoking Cessation

Scottish Office(1995) : *Smoking Cessation and the Dental Team*: £4000

ASH Scotland/PATH (2003) : *Preventing Oral Cancer an intervention in a dental setting* : £130, 113

Invited Lectures

Viv also lectures on Tobacco and Smoking Cessation to various oral health professionals including undergraduates and dentists, dental hygienists and dental nurses, as part of the *NHS Education* CPD and PCD continuing education programmes. Courses have been held so far, in Glasgow, Edinburgh, Dundee and Inverness. Viv has also lectured on the topic at Emerging Trends in Oral Care, Philips Oral Healthcare Symposium 2004, Paris.

